CLINICAL STUDY REPORT: P0501

1 TITLE PAGE

Study Title:	A Multicenter, Randomized, Phase III Registration Trial of Transplantation of omidubicel (NiCord®), *Ex Vivo* Expanded, Umbilical Cord Blood-derived, Stem and Progenitor Cells, versus Unmanipulated Umbilical Cord Blood for Patients with Hematological Malignancies
Study Number:	P0501
Study Phase:	Phase III
Study Design:	Open-label, controlled, multicenter, international, Phase III, randomized study
Product Name:	Omidubicel (NiCord)
Indication:	Patients with hematological malignancies for whom allogeneic stem cell therapy is currently a recommended and potentially life-saving treatment
Principal Investigator(s):	Mitchell Horwitz, MD Duke University Medical Center, NC, U.S. Guillermo F. Sanz, MD, PhD Hospital Universitario y Politecnico La Fe, Spain
Sponsor:	Gamida Cell Ltd. PO Box 34670 Jerusalem 91340 Israel Tel: 972-2-6595666 Fax: 972-2-6595616
Medical Officers:	Einat Galamidi Cohen, MD Vice President Gamida Cell Clinical Development, Medical Lead Radhika Kondapaka, MBBS, RAC The Emmes Company, LLC
Final Date:	23 January 2022

2 SYNOPSIS

<table>
<tr><td colspan="3">NAME OF IND SPONSOR:
Gamida Cell Ltd.</td></tr>
<tr><td colspan="3">NAME OF STUDY DRUG:
Omidubicel (NiCord)</td></tr>
<tr><td colspan="3">Title of Study: A Multicenter, Randomized, Phase III Registration Trial of Transplantation of Omidubicel (NiCord), Ex Vivo Expanded, Umbilical Cord Blood-derived, Stem and Progenitor Cells, versus Unmanipulated Umbilical Cord Blood for Patients with Hematological Malignancies</td></tr>
<tr><td>Study Chairs:</td><td>Mitchell Horwitz, MD
Duke University Medical Center</td><td>Guillermo F. Sanz, MD, PhD
Hospital Universitario y Politecnico La Fe</td></tr>
<tr><td colspan="2">Study Period:
First Enrollment (First patient first visit):
12/20/2016
Last Assessment (Last patient last visit):
04/15/2021
(15 Months Post-randomization)
This report includes data up to 04/29/2021, the data cutoff date, at which point all patients reached 365 Days post-transplant / 15 Months post-randomization</td><td>Phase of Development:
III</td></tr>
<tr><td colspan="3">Objectives:

The objective of this Phase III pivotal study was to compare the safety and efficacy of omidubicel (a single ex vivo expanded cord blood unit [CBU]) transplantation to unmanipulated CBU transplantation in subjects with hematological malignancies following conditioning therapy.

Primary Endpoint:

Assessment of the time to neutrophil engraftment following transplantation.

Secondary Endpoints:

Assessment of three secondary endpoints:
• Incidence of Grade 2/3 bacterial or invasive fungal infections by 100 Days following transplantation
• Days alive and out of hospital in the first 100 Days post-transplantation
• Platelet engraftment by 42 Days post-transplantation

Tertiary Endpoint:
• Non-relapse mortality by 210 Days following randomization

Exploratory Endpoints:
• Neutrophil engraftment by 16 Days following transplantation
• Time from transplantation to platelet engraftment
• Duration of primary hospitalization</td></tr>
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- Non-relapse mortality by 130 Days and 15 Months following randomization
- Overall survival at 210 Days and 15 Months following randomization
- Disease-free survival at 15 Months following randomization
- Neutrophil engraftment by 42 Days following transplantation
- Acute graft-versus-host disease (GvHD) Grade II-IV and III-IV by 100 Days following transplantation
- Chronic GvHD (mild/moderate/severe) by 180 Days and one year following transplantation
- Secondary graft failure by one year following transplantation
- Grade 3 viral infections by 180 Days and one year following transplantation
- Safety and tolerability of omidubicel transplantation
- Relapse by 15 Months following randomization
- Relapse mortality by 15 Months following randomization
- Immune reconstitution at 28, 70, 100, 180, and 365 Days following transplantation
- Supplemental immune reconstitution assessments at a central laboratory (optional)
- Health-related quality of life (QoL)
- Long-term clinical outcomes up to 5 years following transplantation (optional)

Methodology:

This controlled, open-label, multicenter, international, Phase III, randomized study was conducted to compare transplantation of omidubicel to transplantation of one or two unmanipulated, unrelated cord blood units in subjects with hematological malignancies for whom allogeneic stem cell transplant (SCT) is currently a recommended and potentially life-saving treatment, all with required disease features rendering them eligible for allogeneic transplantation.

Number of Subjects (planned and analyzed):
Planned: 120
Analyzed: 125

Diagnosis and Main Criteria for Inclusion:

Subjects aged 12-65 years with a diagnosis of hematological malignancy who are candidates for unrelated cord blood (CB) transplantation with qualifying human leukocyte antigen (HLA)-matched unmanipulated CBUs with sufficient pre-cryopreserved total nucleated cell count and dose, and CD34+ cell dose, as delineated in the study protocol.

Inclusion Criteria:

1. Subjects must have been 12-65 years of age at the time of randomization
2. Patients had one of the following hematological malignancies:
    a. Acute lymphoblastic leukemia (ALL) at one of the following stages:
        i. High-risk first complete morphologic remission (CR1), defined as one or more of the following:
            1. The presence of adverse cytogenetics or adverse molecular changes. Examples of adverse cytogenetics are t(4;11), t(9;22), t(1;19), MLL rearrangements t(11q23) or severe hypodiploid ALL
            2. Extreme leukocytosis at diagnosis (white blood cell (WBC) >30,000/µl for B-ALL or >100,000/µl for T-ALL)

3. Failure to achieve complete morphologic remission after first induction therapy
4. Evidence of minimal residual disease (MRD) at screening by flow cytometry or molecular testing
5. Evidence of slow response to induction therapy, such as peripheral blood leukemic blasts one week after start of induction, or >10% leukemic blasts in bone marrow (BM) 2 weeks after start of induction
6. Age older than 30 years at diagnosis

ii. Second or subsequent complete morphologic remission

b. Acute myelogenous leukemia (AML) at one of the following stages:

i. First complete morphologic remission (CR1) that is NOT considered as favorable risk
Favorable risk was defined as having one or more of the following at diagnosis and absence of MRD at screening:

1. t(8,21) without cKIT mutation
2. inv(16) or t(16;16) without cKIT mutation
3. Normal karyotype with mutated NPM1 and no FLT-3 Internal Tandem Duplication
4. Normal karyotype with double mutated CEBPA
5. Acute Promyelocytic Leukemia (APL) in first or second molecular remission at end of consolidation

ii. Patients in CR1 with one or more of the favorable risk criteria but with additional high-risk features were considered eligible upon consultation with the study chairs.

iii. Second or subsequent remission

c. Chronic myelogenous leukemia (CML) at one of the following phases:

i. Chronic phase with one or more of the following characteristics:

1. Failure to achieve a primary hematologic or cytogenetic response to either nilotinib or dasatinib (following European LeukemiaNet timelines summarized in Protocol Appendix H)
2. Intolerance to/failure of two tyrosine kinase inhibitors (TKI)
3. Any T315I mutation
4. Prior blast crisis

ii. Accelerated phase with one or more of the following characteristics:

1. Newly diagnosed patients who do not achieve an optimal response to TKIs as outlined in the European LeukemiaNet timelines summarized in Protocol Appendix H
2. TKI-treated patients who progress from chronic phase

iii. Prior blast crisis (myeloid or lymphoid) at the time of screening in chronic phase or in complete morphologic or molecular remission

d. CMMoL or myelodysplastic syndrome (MDS)/CMMoL overlap with spleen size <13 cm

e. Myelodysplastic Syndrome (MDS) with history of one or more of the following:

i. International Prognostic Scoring System (IPSS) risk category of INT-1 or greater. MDS patients categorized as INT-1 on primary presentation must have life-threatening neutropenia (absolute neutrophil count (ANC) < 0.5×10^9/L) or thrombocytopenia (platelets < 30×10^9/L).

ii. Revised International Prognostic Scoring System (IPSS-R) risk category of intermediate or greater

f. Biphenotypic/undifferentiated/Prolymphocytic/Dendritic Cell Leukemias and Natural Killer Cell Malignancies in first or subsequent CR, adult T-cell leukemia/lymphoma in first or subsequent CR

g. Lymphoma, meeting one of more of the following criteria:

i. Burkitt's lymphoma in second or subsequent CR
OR

ii. High-risk lymphomas in first CR, including, enteropathy-associated T-cell lymphoma, or hepatosplenic γδ T-cell lymphoma
OR

iii. Chemotherapy-sensitive (defined as at least stable disease) lymphomas that have failed at least one prior regimen of multi-agent chemotherapy and are not candidates for an autologous transplant.
(*Patients with chronic lymphocytic leukemia (CLL) were not eligible regardless of disease status*)

3. CBU criteria as described in Section 9.4.4 and summarized below.

a. HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. High-resolution matching was required for HLA class II. At least one allele match at DRB1 was required.

b. The CBU intended for expansion was required to contain a pre-cryopreserved (post-processing) total CD34+ cell count of at least 8×10^6, as well as a pre-cryopreserved (post-processing) total nucleated cell count of at least 1.8×10^9, and a total nucleated cell dose of at least 1.5×10^7 total number of viable cells (TNC)/kg body weight

c. If the CBU was HLA-matched at 5-6/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $<2.5\times10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.2\times10^5$ CD34+ cells/kg, a second CBU was required to be added for the control arm, as a double cord blood transplantation (CBT).

d. If the CBU was HLA-matched at 4/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $<3.5\times10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $<1.7\times10^5$ CD34+ cells/kg, a second CBU was required to be added for the control arm, as a double CBT.

e. In case of double CBT in the control arm: The two CBUs were required to have a combined pre-cryopreserved (post-processing) total nucleated cell dose of $\geq3\times10^7$ TNC/kg.

4. Patients who were to start conditioning prior to omidubicel release for infusion (i.e., omidubicel arrival on site in adequate condition) had to have an additional partially HLA-matched CBU, reserved as a backup to the omidubicel arm in case of production failure. The backup CBU had to be HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. A second backup CBU was recommended to be added in the below cases:
    a. If the backup CBU was HLA-matched at 5 or 6/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $<2.5\times10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $<1.2\times10^5$ CD34+ cells/kg
    b. If the backup CBU was HLA-matched at 4/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $<3.5\times10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $<1.7\times10^5$ CD34+ cells/kg

    In case of two backup CBUs, the second backup CBU had to be HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. The backup CBUs were recommended to have a combined pre-cryopreserved (post-processing) total nucleated cell dose of at least 3×10^7 TNC/kg.
5. Patient's Performance score ≥70% by Karnofsky or Lansky
6. Patient had sufficient physiologic reserves including:
    a. Cardiac: Left ventricular ejection fraction (LVEF) of ≥40% by echocardiogram, radionuclide scan or cardiac MRI, or left ventricular shortening fraction ≥ 29%.
    b. Pulmonary function tests (PFT) (prior to treatment with bronchodilators) demonstrating FVC and FEV1 of >50% of predicted for age and (carbon monoxide diffusing capacity) cDLCO > 50% of predicted for patients in whom pulmonary function testing could be performed (If PFT testing included the use of bronchodilators, then the baseline results during testing prior to the administration of any medications should have been used when determining eligibility).
    c. Renal: Creatinine clearance test (by Cockcroft-Gault equation) ≥60 mL/min
    d. Hepatic: Serum Bilirubin < 2.0 mg/dl; Hepatic transaminases alanine transaminase and aspartate transaminase (ALT and AST) < 3 x upper limit of normal range
7. Females of childbearing potential, defined as any female who had experienced menarche and was not postmenopausal (defined as not having a menstrual period for at least 24 months) or permanently sterilized (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy), agreed to use an appropriate method of contraception from at least 7 days prior to conditioning regimen therapy until completion of follow-up procedures. An appropriate method of contraception was defined as one that results in a low failure rate (i.e., less than 1 percent per year) when used consistently and correctly, such as implants, injectables, combined oral contraceptives, intrauterine contraceptive devices (IUDs), true sexual abstinence (when this was in line with the preferred and usual lifestyle of the patient), or a vasectomized partner.
8. Patient (or legal guardian) signed the written informed consent after being aware of the nature of the patient's disease and willingly consented to the treatment program after having been informed of alternative treatments, potential risks, benefits, and discomforts.

Exclusion Criteria:

1. MDS or CML with "marked" or "3+" fibrosis

2. Chronic lymphocytic leukemia (CLL)
3. Fewer than 21 days had elapsed since initiation of the patient's last chemotherapy cycle and the initiation of the SCT preparative regimen (radiotherapy, intrathecal agents, hydroxyurea, TKI, hypomethylating agents, rituximab, blinatumomab and lenalidomide are not considered chemotherapy)
4. Persistent clinically significant toxicities that, in the investigator's opinion, made the patient unsuitable for transplant
5. Evidence of donor specific anti-HLA antibodies to the selected treatment CBU #1 (MFI>3000 to HLA-A, B, C, or DRB1)
6. Evidence of HIV infection or HIV positive serology
7. Evidence of active Hepatitis B or Hepatitis C as determined by serology or polymerase chain reaction (PCR)
8. Pregnancy, as indicated by a positive serum or urine human chorionic gonadotrophin (HCG) test, or lactation
9. Active malignancy other than that for which the umbilical CB transplant was being performed within 12 months of enrollment. Fully resected cutaneous squamous cell or basal cell carcinoma or cervical carcinoma in situ within 12 months of enrollment was permitted.
10. Evidence of uncontrolled bacterial, fungal or viral infections or severe concomitant diseases, which in the judgment of the Principal Investigator indicated that the patient could not tolerate transplantation
11. Patients with presence of leukemic blasts in the central nervous system (CNS)
12. Patients with an 8/8 allele level HLA-matched and readily available related or unrelated donor (whose stem cells could be collected in a timely manner without jeopardizing recipient outcome). Patients who had haploidentical related donors or syngeneic donors were not excluded.
13. Prior allogeneic hematopoietic SCT
14. Allergy to bovine products, gentamicin, or to any other product that may interfere with the treatment
15. Psychologically incapable of undergoing bone marrow transplant (BMT) with associated strict isolation or documented history of medical non-compliance and/or psychiatric illness and/or social situations that would limit compliance with study requirements
16. Enrolled in another interventional clinical trial or received an investigational treatment within 30 days prior to the anticipated date of randomization, unless documented approval obtained from Sponsor prior to randomization

Test Product, Dose and Mode of Administration:

Omidubicel (NiCord)

Dosage Form:

- Cultured Fraction (CF): $\geq 8.0 \times 10^8$ TNC in approximately 20 mL of cryopreservation solution frozen in liquid nitrogen (LN) reconstituted to 100 mL thawed.
- Non-Cultured Fraction (NF): $\geq 4.0 \times 10^8$ TNC in approximately 10 mL of cryopreservation solution frozen in LN reconstituted to 50 mL thawed.

Mode of Administration: Intravenous (IV)

Dose Regimen:

One-time administration; the CF and NF were transfused via the patient's central venous catheter as per site practice. The CF was infused first, followed immediately (up to 1 hour) by the infusion of the NF. Total duration of CF infusion targeted a maximum of 2 hours from end of thaw to end of infusion, taking into account the minimal infusion time according to the Certificate of Analysis (CoA). Total duration of NF infusion should not have exceeded 1 hour from end of thaw to end of infusion, considering the minimal infusion time according to the CoA. Infusion of CF and NF were to target a rate of 5 cc/kg/hr with a maximal rate of 10 cc/kg/hr. The CF and NF were to be infused as soon as possible after thaw.

Duration of Treatment:

Omidubicel was given as a single dose consisting of two fractions on a single day. Dose regimen for omidubicel was followed as described above. For the control arm, one or two unmanipulated CBU(s) were given on a single day per institutional procedures.

Criteria for Evaluation:

There is substantial overlap between efficacy and safety evaluations in transplant studies. Therefore, some outcomes are presented in both the efficacy and safety sections of this report. For such outcomes, the efficacy section focuses on the evaluation of the specific endpoints and any significant differences between treatment arms whereas the safety section provides more granular details about types of events and individual descriptions of significant events.

Efficacy:

The primary efficacy endpoint was to assess the time to neutrophil engraftment following transplantation, defined as achieving an ANC $\geq 0.5 \times 10^9$/L on 3 consecutive measurements on different days with subsequent donor chimerism (≤10% host cells by peripheral blood chimerism or BM chimerism if peripheral blood chimerism was not available). Moreover, the day of neutrophil engraftment was designated as the first of the three consecutive measurements and must have occurred on or before 42 days post-transplantation and prior to infusion of any additional stem cell product.

Secondary endpoints included a comparison of omidubicel versus unmanipulated CBU treated patients for the following endpoints:

- Incidence of Grade 2/3 bacterial or invasive fungal infections by 100 Days following transplantation
- Days alive and out of hospital in the first 100 Days following transplantation
- Platelet engraftment by 42 Days following transplantation

Tertiary endpoint

- Non-relapse mortality by 210 Days following randomization

Additional endpoints included:

- Incidence of viral infections
- Time from transplant to neutrophil and platelet engraftment
- Duration of primary hospitalization
- Overall and disease-free survival
- Incidence of relapse and relapse mortality
- Immune reconstitution
- Health-related quality of life

Safety:

The safety endpoints (safety and tolerability of omidubicel transplantation) included the following:

- Infusion reactions
- Primary and secondary graft failure
- Infections (types, severity, treatment)
- Incidence and severity of acute and chronic GvHD
- Other SAEs frequency, severity

Statistical Methods:

The study compared the distribution of times to engraftment in the omidubicel vs control groups. The comparison between omidubicel and unmanipulated CBU was based on a Mann-Whitney test statistic, which was equivalent to using a Gehan-Wilcoxon alternative with the following events treated as competing risks:

- Failure to receive a transplant within 90 Days following randomization (counted as a competing risk event at Day 0)
- Relapse
- Death
- Second transplant.

Follow-up was between Day 0 and Day 42 following transplant. Those not achieving engraftment by Day 42 were censored on Day 43 (and were viewed as never achieving engraftment). The estimated cumulative distribution of the times, as well as the median times to engraftment were presented for each treatment group. The statistical test was based on the rerandomization distribution in view of using the minimization method for treatment allocation (Section 9.7). Two secondary analyses of this primary endpoint were conducted using the same statistical methods: (i) on the as-treated population (AT) (and excluding patients who did not receive a transplant), and (ii) on the as-treated population who achieved neutrophil engraftment. In a third secondary analysis, time to neutrophil engraftment in the two treatment groups was compared by a LogRank test statistic in the intention-to-treat (ITT) population.

Thus, the primary analyses of the primary, secondary and tertiary endpoints were conducted on the ITT population, i.e., all patients randomized were included and their group membership was the same as the group to which they were randomized, regardless of what treatment they received. Subgroup analyses according to age, disease risk group, disease (ALL, AML, MDS, CML and lymphoma), gender, race/ethnicity, geographical region, and intention to perform single/double CBT were performed as supportive analyses for both primary and secondary endpoints.

Method of allocation: Stratification by minimization

Patients were randomized to treatment by omidubicel or by unmanipulated CBU (single or double unit). The method of minimization was used to provide balanced treatment assignment across selected factors of prognostic importance including: treatment center, age, and disease risk group. A random element with a pre-selected probability of 0.9 was used in the allocation method. Statistical inferences from all ITT analyses were based on the re-randomization distribution.

Results:

One hundred and twenty-five patients were randomized in a total of 33 centers in seven countries. Among randomized patients, 87 (70%) were enrolled in the United States, 15 (12%) from Spain, nine (7%) from Singapore, and six (5%) from the Netherlands. All other countries contributed less than 5% of patients each. The randomization was conducted successfully, as demonstrated by well-balanced patient characteristics across the two study arms in term of age, primary diseases, disease risk and specific clinical site supportive care guidelines.

Demographics and baseline disease characteristics were well-balanced in the two arms, specifically for those factors used for minimization, and were similarly distributed across the ITT and AT populations. The median age of patients in the study was 40 years for the omidubicel arm and 43 years for the unmanipulated CBU arm. Of note, the study population was ethnically diverse, with over 40% identified as non-Caucasian. Acute leukemias (AML and ALL) were the most common indications for transplant, and most patients had moderate to high-risk disease. Patient ages ranged from 13 to 65 years, and patients with weights up to over 130 kg were enrolled in both arms, reflecting a study population that is representative of the general population eligible for transplant.

Efficacy Results:

Results of the primary endpoint demonstrated that 88.7% (n=55) of the omidubicel ITT population reached neutrophil engraftment by Day 42 post-transplantation.

The study met its primary endpoint, demonstrating by ITT analysis that the time to engraftment was shortened by omidubicel transplantation compared to unmanipulated CBU transplantation ($p<0.001$). Patients in the omidubicel group reached engraftment earlier than patients in the unmanipulated CBU group, as the median time to neutrophil engraftment was 12 days (95% CI 10-14) for the omidubicel group in contrast to 22 days (95% CI 19-25) for the unmanipulated CBU group. Secondary sensitivity analyses of the primary endpoint support the overall conclusions from the primary endpoint analyses as results regarding time to neutrophil engraftment were identical. A secondary sensitivity analysis of the primary endpoint stratified by disease indicated the difference in time to neutrophil engraftment was still statistically significant ($p<0.001$). Ninety-six percent of patients who received omidubicel (As-Treated (AT) population) achieved successful neutrophil engraftment by 42 days post-transplant, compared to 89% of patients who received unmanipulated CBU.

The study secondary endpoints provided support to the clinical benefit by demonstrating an improvement in the incidence of platelet engraftment by Day 42 post-transplant (55% vs. 35%; $p=0.028$), a reduction in Grade 2-3 bacterial and invasive fungal infections by 100 Days post-transplant (39% vs. 60%; $p=0.016$), and a higher probability of days alive and out of hospital within the first 100 days post-transplant (60.5 days vs. 48 days; $p=0.005$), all analyzed in the ITT population. These endpoints all maintained statistical significance ($p<0.05$) following multiple comparison adjustments.

By 210 days post-randomization, non-relapse mortality was 11% for the omidubicel arm compared to 24% for the unmanipulated CBU arm ($p=0.09$). By 15 Months post-randomization, overall survival was 73% for the omidubicel arm and 60% for the unmanipulated CBU arm ($p=0.13$).

At 15 months after randomization, encompassing at least 1 year following transplantation, NRM for the omidubicel arm was 15% compared to 29% for unmanipulated CBU (p=0.068).

At 15 months following randomization overall survival for omidubicel was 73% compared to 60% for unmanipulated CBU (p=0.134). Disease-free survival (DFS) was similar between treatment arms, 63% for omidubicel and 56% for unmanipulated CBU (p=0.448). The cumulative incidence of relapse was 23% for omidubicel and 16% for unmanipulated CBU (p=0.320).

Safety Results:

At least one treatment emergent adverse event (TEAE) was reported in every patient, and a Grade 3-5 adverse event (AE) was reported in nearly all patients (98% of omidubicel [n=51] and 95% of unmanipulated CBU patients [n=52]).

For patients treated with omidubicel, the most common Grade 3-5 AEs by preferred term were pain in 17 (33%) patients, mucosal inflammation in 16 (31%) patients, and hypertension in 13 (25%) patients. For patients treated with unmanipulated CBU, the most common Grade 3-5 AEs were hypertension in 21 (38%) patients, mucosal inflammation in 19 (34%) patients, gastrointestinal toxicity in 19 (34%) patients. Treatment-emergent SAEs were reported in 90% (n=47) of omidubicel patients and 91% (n=51) of unmanipulated CBU patients. The most common suspected adverse reaction was GvHD. Other suspected AEs included hypertension (4% of omidubicel patients and 16% of unmanipulated CBU patients), graft failure (4% of omidubicel patients and 9% of unmanipulated CBU patients), pain (6% of omidubicel patients and 2% of unmanipulated CBU patients), dyspnea (2% of omidubicel patients and 7% of unmanipulated CBU patients), hypoxia (2% of omidubicel patients and 4% of unmanipulated CBU patients) and thrombotic microangiopathy (4% of unmanipulated CBU patients).

There were 21 related treatment-emergent SAEs in patients who received omidubicel versus 23 related treatment-emergent SAEs in patients who received unmanipulated CBU. Overall, 46% (n=24) and 52% (n=29) of patients had TEAE related to omidubicel or unmanipulated CBU, respectively. In addition, 23% (n=12) of omidubicel patients had a treatment-emergent death whereas 36% (n=20) of unmanipulated CBU patients had a treatment-emergent death.

The main conclusions of the safety analyses indicate a similar frequency and severity of Grade 3+ infusion reactions observed in patients treated with omidubicel compared to unmanipulated CBU. Overall the frequency of Grade 3 or higher TEAEs was either similar or lower for omidubicel than for unmanipulated CBU. Patients randomized to omidubicel had a lower incidence of Grade 2-3 bacterial or invasive fungal infections by 100 Days following transplantation compared to patients randomized to unmanipulated CBU (39% vs. 60%; ITT population). The risk ratio for total infections, bacterial infections or viral infections was significantly lower for omidubicel compared to unmanipulated CBU, irrespective of disease severity. Patients transplanted with omidubicel had fewer infectious SAEs and a lower incidence of fever and sepsis.

A review of Grade 3 or higher TEAEs noted a higher frequency of pain reported for the omidubicel recipients, however further interrogation of the safety data did not indicate an underlying safety event that occurred at a higher frequency or severity for omidubicel recipients. A higher frequency and severity of respiratory events was reported in the unmanipulated CBU group, especially respiratory failure. In further analysis, the majority of these events occurred concurrently or were attributable to infectious complications.

The outcomes of acute and chronic GvHD demonstrated no statistically significant difference between patients transplanted on the omidubicel or the unmanipulated CBU groups. These rates are consistent with those observed with other graft modalities used in hematopoietic stem cell transplantation (HSCT). There was no significant difference in the risk of relapse among the two arms. No cases of new malignancies of donor origin were reported in the study.

Discussion and Conclusions:

Allogeneic HSCT following myeloablative conditioning is associated with a well-described and pattern of severe, life-threatening or fatal complications. Many of the toxicities associated with HSCT are related to the duration of hematopoietic recovery after transplant. The rapid rate of hematopoietic recovery observed in patients transplanted with omidubicel was associated with clinically meaningful improvement in infection rates and duration of hospitalization. The overall pattern and severity of AEs, as well as treatment-related mortality, were more favorable in patients treated with omidubicel than in those treated with unmanipulated CBU.

Patients transplanted with omidubicel are potentially at risk of developing toxicities which may occur following HSCT with other graft sources. Safety data demonstrated that safety outcomes were consistent with those observed with myeloablative HSCT with other graft sources.

This study was designed to compare the efficacy and safety of omidubicel with the most relevant comparator, unmanipulated CB, from which it is derived. Both study arms utilized the same type, quantity and quality of donor stem cells derived from CBUs selected prior to randomization.

As this study was conducted in an orphan patient population, it was imperative to investigate the safety and tolerability of omidubicel in a diverse population representative of patients with high-risk hematologic malignancies. Patients were randomized by minimization to balance the groups for the most important prognostic factors impacting treatment outcomes. Considering the diversity of the patient population in terms of age, primary diseases, disease risk and specific clinical site supportive care guidelines, randomization was conducted successfully, as demonstrated by well-balanced patient characteristics across the two study arms. As noted, the diversity of the patient population was substantial, with ages spanning 13-65 years, weights of 43-134 kg, 6 major diagnoses with varying disease risk and numerous specific diseases. This wide range reflects a population that is representative of the general population eligible for transplant. Importantly, the study population was ethnically diverse, with over 40% identified as non-Caucasian. While many Caucasian patients are able to find suitable donors within the registries, these ethnically diverse populations have a much lower success rate and represent the highest need for better graft alternatives.

Most importantly, the primary endpoint was a clinically meaningful and objective endpoint, as reflected by serial daily blood counts, and the median time to engraftment of 12 days represents an effect of clinical significance. The primary analysis of the primary endpoint was an ITT analysis, encompassing all randomized patients according to their originally assigned treatment. As such, although the analysis assesses a post-transplant measure, it includes all the treatment failures, treatment deviations and patients who were not treated. This approach minimized the risk of bias due to knowledge of the treatment assignment, given that patients and clinical study sites were not blinded to treatment allocation. Furthermore, this approach preserved the prognostic balance across the two arms. While the three-week duration required for omidubicel production could have been associated with an increased risk of relapse prior to transplant in this arm, the ITT analysis

reflected a comprehensive assessment of the treatment benefit and revealed no such risk. Overall results demonstrate omidubicel has the potential to provide a life-saving graft for a diverse group of patients in need of HSCT. This randomized, well controlled study met its primary endpoint, demonstrating a significant improvement in time to neutrophil engraftment. The primary endpoint was supported by secondary endpoints that demonstrated superiority in Grade 2/3 bacterial and invasive fungal infections, days alive and out of hospital, and platelet engraftment following transplantation. The secondary endpoints reflected the significant risk of clinical sequelae of delayed hematopoietic recovery, and results from the secondary endpoint analyses support the primary endpoint analysis, providing further evidence of the overall clinical benefit of omidubicel.

Date of the Report: 23 January 2022

MEMORANDUM
MODIFICATIONS TO CSR DATED 28 NOVEMBER 2021

The modifications made to the previous CSR version issued on 28 November 2021 are of the following types:

- Update of incorrect numbering of Tables and Figures in the section 14 standalone document:
    - The in-text index of section 14 was updated accordingly, with accurate numbering and Tables/Figures titles as they appear in the separated document containing those Tables and Figures.
- Addition of a few tables in the section 14 standalone document, that were mistakenly omitted in the previous CSR version
    - The in-text index of section 14 was updated accordingly
- Addition of two listings in the section 16.2 standalone document, that were mistakenly omitted in the previous CSR version
- Update of incorrect or missing reference numbers in the text (references to Tables/Figures included in section 14 or Listings included in section 16.2)
- Wording adaptation in section 11.4.1.1 “Primary Endpoint: Time to Neutrophil Engraftment Following Transplantation”: “patient **receiving** (omidubicel/unmanipulated) CBU” replaced by “patient in the (omidubicel/unmanipulated CBU) **arm**”, to accurately reflect the analyzed population (intent-to-treat) based on the randomization arm and not on the treatment received. This modification doesn’t affect the content of the analysis itself.

Those modifications are considered as minor none of them affect the content of the CSR synopsis. Therefore, no standalone synopsis was issued for this updated CSR. The standalone synopsis dated 28 November 2021 serves also as the standalone synopsis of this corrected CSR version.

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4 LIST OF ABBREVIATIONS

Abbreviation	Definition
Ab	Antibody
ABG	Arterial blood gas
ABMT	Autologous bone marrow transplantation
ABW	Actual body weight
AC/PC	Assist controlled/pressure controlled
AC/VC	Assist controlled/volume controlled
ACE	Angiotensin-converting enzyme
AE	Adverse Event
AEP	ANC-Engrafted Population
A-fib	Atrial fibrillation
ALL	Acute Lymphoblastic Leukemia
ALT	Alanine transaminase
AMET	Adult Medical Emergency Team
AML	Acute Myelogenous Leukemia
ANC	Absolute neutrophil count
Anti-TNF	Anti-tumor necrosis factor
AP/PA position	Anterior posterior/posterior anterior position
APL	Acute Promyelocytic Leukemia
ASHI/EFI	American Society for Histocompatibility and Immunogenetics/European Federation for Immunogenetics
AST	Aspartate transaminase
AT	As-Treated
AUC	Area under the curve
BAL	Bronchoalveolar lavage
B Cell	Bone marrow lymphocyte cells (CD19+)
BID	Twice a day
BiPAP	Bilevel positive airway pressure
BM	Bone marrow
BMT	Bone marrow transplant
BMTS	Bone marrow transplantation subscale
BNP	B-type natriuretic peptide
BPM	Beats per minute
BSA	Body surface area
CALG-B	Cancer and Leukemia Group B
CB	Cord blood
CBB	Cord blood bank
CBC	Complete blood count
CBT	Cord blood transplant/transplantation
CBU	Cord blood unit
cDLCO	Corrected diffusing capacity of the lungs for carbon monoxide
CF	Cultured fraction
CFU	Colony-forming units

Abbreviation	Definition
CHR	Complete hematologic response
CI	Cumulative incidence
CIBMTR	Center for International Blood and Marrow Transplant Research
CK-MB	Creatine kinase-MB
CML	Chronic myelogenous leukemia
CMR	Complete molecular response
CMMoL	Chronic myelomonocytic leukemia
CMV	Cytomegalovirus
CNS	Central nervous system
CoA	Certificate of Analysis
CoNS	Coagulase-negative staphylococci
CPK	Creatinine phosphokinase
CR	Complete remission
CRA	Clinical Research Associate
(e-) CRFs	(Electronic) Case Report Forms
CRF	Chronic renal failure
Cri	Complete response-incomplete
CRO	Contract Research Organization
CSA	Cyclosporin A
CSF	Cerebrospinal fluid
CT	Computerized tomography
CTA	Computerized tomography – angiography
CTCAE	Common Terminology Criteria for Adverse Events
CVVH	Continuous veno-venous hemofiltration
CXR	Chest X-ray
CY	Cyclophosphamide administration
(c/p/m) CyR	(Complete/Partial/Minor) cytogenetic response
DAH	Diffuse alveolar hemorrhage
DCC	Data Coordinating Center
DCBT	Double cord blood transplant
DFS	Disease-free survival
DLCO	Diffusing capacity of the lungs for carbon monoxide
DMC	Data Monitoring Committee
DNA	Deoxyribonucleic acid
DNR-CC	Do not resuscitate – comfort care
DRI	Disease risk index
EBMT	European society for Blood and Marrow Transplantation
EBV	Epstein-Barr virus
EC	Ethics Committee
ECG	Electrocardiogram
ECP	Extracorporeal photopheresis
ED	Emergency department
EDC	Electronic data capture
EEG	Electroencephalogram

Abbreviation	Definition
EGD	Esophagogastroduodenoscopy
EKG	Electrocardiography
EMA	European Medicines Agency
EVCTM	EudraVigilence Clinical Trial Module
FACS	Fluorescence-activated cell sorting
FACT-BMT	Functional Assessment of Cancer Therapy – Bone Marrow Transplant
FACT-G	Functional Assessment of Cancer Therapy – General
FBS	Fetal bovine serum
FEV1	Forced expiratory volume in one second
FISH	Fluorescent i*n* s*itu* hybridization
FLT3	FMS-like tyrosine kinase
FLT3-L	FLT-3-ligand
FPQC	Final process quality controls
FVC	Forced vital capacity
FWEs	Family-wise error rate
GC	Gamida Cell
GCP	Good Clinical Practice
G-CSF	Granulocyte colony-stimulating factor
GERD	Gastroesophageal reflux disease
GFR	Glomerular filtration rate
GMF	Grocott methenamine silver
GvHD	Graft-versus-host disease
Hb	Hemoglobin
HCG	Human chorionic gonadotropin
HCT	Hematopoietic cell transplantation
HCV	Hepatitis C virus
H-CVAD	Hyper-cyclophosphamide, vincristine sulfate, doxorubicin hydrochloride, and dexamethasone
HBcAb	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
HHV	Human herpesvirus
HHV-6	Human herpesvirus 6
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HPC	Hematopoietic progenitor cells
HRQoL	Health-related quality of life
HRCT	High-resolution computed tomography
HSC	Hematopoietic stem cells
HSCT	Hematopoietic stem cell transplantation
HSPCs	Hematopoietic stem/progenitor cells
HSV	Herpes simplex virus
HTLV	Human T-lymphotropic virus
IB	Investigator Brochure

Abbreviation	Definition
IBW	Ideal body weight
IC	Informed consent
ICH	International Conference on Harmonization
ICU	Intensive care unit
ID	Identity document
Ig	Immunoglobulin
IL6	Interleukin 6
IMP	Investigational Medicinal Product
IND	Investigational New Drug
IPQC	In-process quality controls
IPS	Idiopathic pneumonia syndrome
IPSS	International prognostic scoring system
IRB	Institutional Review Board
ISO	International Organization for Standardization
IT	Intrathecal
ITP	Immune thrombocytopenic purpura
ITT	Intent-to- treat
IUD	Intrauterine contraceptive device
IV	Intravenous
IVIG	Intravenous immunoglobulin
LRI	Lower respiratory infection
LVEF	Left ventricular ejection fraction
MAP	Mean arterial pressure
MARTs	Mono-ADP-ribosyl transferases
MDS	Myelodysplastic syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MFI	Mean fluorescence intensity
MICU	Medical intensive care unit
MLL	Myeloid/lymphoid leukemia
MM	Medical Monitor
MMF	Mycophenolate mofetil
MMR	Major molecular response
MMRM	Mixed effect models with repeated measures
MMUD	Mismatched unrelated donor
MRD	Minimal residual disease
MRI	Magnetic resonance imaging
MRU	Medical resources utilization
MS	Mass spectrometry
MS CA	Member States Competent Authority
MUD	Matched unrelated donor
MUGA	Multigated acquisition scan
MVO2	Myocardial volume oxygen
N/A	Not applicable
NAD+	Nicotinamide adenine dinucleotide

Abbreviation	Definition
NAM	Nicotinamide
NC	Nasal canula
NCI	National Cancer Institute
NF	Non-cultured fraction
NIH	National Institutes of Health
NK cell	Natural killer cytotoxic lymphocyte cells (CD56+/CD16+cells)
NOS	Not otherwise specified
NP	Nurse practitioner
NRM	Non-relapse mortality
NT Pro BNP	N-terminal pro B-type natriuretic peptide
OOS	Out of specification
PA	Physician Assistant
PaO2	Partial pressure of oxygen
PARPs	Poly-ADP-ribose polymerases
PB	Peripheral blood
PBSC	Peripheral blood stem cell
PCP	Pneumocystis pneumonia
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PEP	Platelet-Engrafted Population
PET	Positron emission tomography
Ph+	Philadelphia chromosome +
PI	Principal Investigator
PIP	Peak inspiratory pressure
PMN	Polymorphonuclear leukocytes
PNA	Pneumonia
PO	By mouth, or oral administration of a drug
POMP	Prednisone +vincristine + methotrexate + 6-mercaptopurine
PRBC	Packed red blood cells
PSV	Pressure support ventilation
PT	Preferred term
PTLD	Post-transplant lymphoproliferative disorder
PTX	Pneumothorax
QC	Quality control
QoL	Quality of life
QP	Qualified person
RBC	Red blood cell
Rh	Rhesus factor
RPR	Rapid plasma reagin
RR	Respiratory rate
RSV	Respiratory syncytial virus
RUQ	Right upper quadrant
RVR	Rapid ventricular response
SAE	Serious Adverse Event

Abbreviation	Definition
SAH	Subarachnoid hemorrhage
SAP	Statistical Analysis Plan
SC	Subcutaneous
SCD	Sickle cell disease
SCF	Stem cell factor
SCID	Severe combined immunodeficiency
SCT	Stem cell transplant
SLM	Study Logistics Manager
SOC	System Organ Class
SOP	Standard Operating Procedures
SP	Safety Population
SPD	Sum of the product diameter
SPRT	Sequential probability ratio test
SRC	SCID repopulating cells
SUSAR	Suspected Unexpected Serious Adverse Reaction
TBI	Total body irradiation
T-CELL	Thymus derived lymphocytes (CD3+ cells; CD4+/CD8+ cells)
TCR-B	T-Cell receptor beta
TCR-G	T-Cell receptor gamma
TDM	Therapeutic drug monitoring
TID	Three times a day
TKI	Tyrosine kinase inhibitor
TNC	Total nucleated cell count
TP	Transplanted population
TPO	Thrombopoietin
TRM	Transplant-related mortality
TV	Tidal volume
UA	Urinalysis
UCBU	Unmanipulated cord blood unit
VAP	Ventilator-associated pneumonia
VBG	Venous blood gas
VRE	Vancomycin-resistant enterococcus
VZV	Varicella zoster virus
WBC	White blood Cell
WOB	Work of Breathing
XR	X-Ray

5 ETHICS

5.1 Institutional Review Board (IRB) or Independent Ethics Committee (IEC)

Institutional Review Board (IRB)/Ethics Committee (EC) approval of the protocol, informed consent forms (ICF), and patient information and/or advertising as relevant was obtained prior to the authorization of omidubicel shipment to a study site and prior to any study procedure was being conducted. All amendments to the protocol received IRB/EC approval prior to implementation of any changes. Detailed IRB/EC information is provided in Appendix 16.1.3.

5.2 Ethical Conduct of the Study

This study was conducted in accordance with the ethical principles originating from the Declaration of Helsinki, current Good Clinical Practice (GCP), and in compliance with Federal and local regulatory requirements.

5.3 Patient Information and Consent

The requirements of informed consent were in accordance with the current version of Declaration of Helsinki. Each patient eligible for the study was properly informed of the purpose of the study and of any anticipated AEs that might be encountered with the study medication. Each subject had the opportunity to ask questions and receive answers concerning all portions of the conduct of the study. A signed and dated, written ICF was obtained from all patients or their authorized representative before they were entered into the study. Sample ICFs can be found in Appendix 16.1.3.

6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

6.1 Administrative Structure at the Clinical Sites

Lead Site: Duke University Medical Center, NC, U.S.
Principal Investigator: Mitchell Horwitz, MD

Lead Site: Hospital Universitario y Politecnico La Fe, Spain
Principal Investigator: Guillermo F. Sanz, MD, PhD

Thirty-three clinical sites enrolled patients into this study. Curriculum vitae of Principal Investigators (PIs) can be found in Appendix 16.1.4.

The following Investigator / Study Coordinator meetings / Webcasts were held during the study for the purpose of training all participating investigators and study coordinator/study nurses on the procedures, tests and evaluations to be used, conducted or assessed in the study (Table 1):

Table 1: List of Investigators/Study Coordinators Meetings Held during the Study

Type of meeting	Date	Location
Investigator Meeting	04DEC2016	San Diego, U.S.
Study Coordinators Meeting	20FEB2018	Salt Lake City, U.S.
Study Coordinators Meeting	21MAR2018	Lisbon, Portugal
Investigator and Study Coordinators Meeting	05NOV2018	Valencia, Spain
Investigator Meeting	28–29JAN2019	Paris, France
Study Coordinators Meeting	03-04APR2019	St. Louis, USA
Investigator Meeting	29APR2019	Tel Aviv, Israel
Webcast for investigators- Phase 3 study	11SEP2019	Webcast Meeting
Webcast for investigators Phase 3 Readout	20/22MAY2020	Webcast Meeting

6.2 Administrative Structure for the Trial

Principal Investigator (s)	Mitchell Horwitz, MD Duke University Medical Center, NC, U.S. Guillermo F. Sanz Hospital Universitario y Politecnico La Fe, Spain
Sponsor	Lonza, 8830 Biggs Ford Rd., Walkersville, MD 21793 Gamida Cell
Manufacturing Sites including Packaging and Labeling	Lonza Walkersville, MD, U.S. Gamida Cell, Jerusalem, Israel
Sponsor Medical Officer Monitor	Einat Galamidi Cohen, M.D
CRO Medical Monitor Officer	Radhika Kondapaka, MBBS, RAC The Emmes Company, LLC

Principal Study Statistician	Laurence S. Freedman, PhD. Gertner Institute for Epidemiology and Health Policy Research Sheba Medical Center
CRO Lead Statistician	Beth Blackwell, PhD The Emmes Company, LLC
Lead Data Management, Monitoring, Pharmacovigilance, and Biostatistical Services Organization	The Emmes Company, LLC 401 N Washington St #700 Rockville, MD 20850
Collaborating CROs Providing Study Monitoring	Experior SL Chiltern International Ltd./Covance Inc. Pharm-Olam LLC
Collaborating Pharmacovigilance Organization	Voisin Consulting Life Sciences (VCLS)
Regulatory Submissions (Including Clinical Trials Applications and adverse events reporting)	U.S. FDA: Gamida Cell U.K. MHRA: VCLS Spain AEMPS: VCLS Netherlands: Experior SL Singapore HSA: Chiltern International Ltd./Covance Inc. Brazil: Pharm-Olam LLC Israel: Gamida Cell
Report Author	David Peel, MS The Emmes Company, LLC
Study Monitoring Organization	The Emmes Company, LLC
Clinical and Specialty Laboratories	Immune Reconstitution samples for the sub-study were processed at Covance CCLS Rue Moïse-Marcinhes 7, 1217 Meyrin, Geneva Switzerland, CH

A Data Monitoring Committee (DMC) was used for this study in order to review the progress of the trial during the enrollment of subjects on a regularly scheduled basis and as requested on an ad hoc basis to ensure that patient safety was not being compromised. Six meetings were held through the accrual period. Data reports reviewed by the committee, meeting minutes and recommendations can be found in Appendix 16.1.9.1.

7 INTRODUCTION

Successful blood and marrow transplantation requires the infusion of a sufficient number of hematopoietic stem/progenitor cells (HSPCs) capable of both homing to the bone marrow and regenerating a full array of hematopoietic cell lineages with early and late repopulating ability in a timely fashion (Cottler-Fox, Lapidot et al. 2003).

Although several options for a stem cell donor for transplantation exist, each option has limitations , therefore these patients still have a serious unmet medical need (Grewal, Barker et al. 2003). HLA-matched donors, whether related or unrelated, are often not available or difficult to procure in a timely manner, especially for diverse ethnic/racial groups (Barker, Krepski et al. 2002, Grewal, Barker et al. 2003, Eapen and Wagner 2010, Ballen, Koreth et al. 2012, Iori, Valle et al. 2012). Alternative donor sources, including mismatched unrelated donor (MMUD), haploidentical (haplo)–related donor and umbilical CB, are partially HLA-mismatched (Solh 2014).

Umbilical CB has been used clinically over the last 25 years for the treatment of diverse life-threatening diseases such as hematological malignancies and genetic blood disorders. However, despite the advantages in the use of CBT, its use, especially in adults and adolescents, is limited. The medical need for suitable allogeneic grafts remains insufficiently met because of the delayed hematopoietic recovery in recipients of CBT, with a related increased risk of life-threatening or fatal sequelae (Brunstein, Gutman et al. 2010, Eapen, Rocha et al. 2010, Ruggeri, Labopin et al. 2014, Barker, Fei et al. 2015). Delayed hematopoietic recovery can result in an increased occurrence or higher severity of infections after transplantation. These infections sometimes lead to substantial organ damage, which may be irreversible, and also death. Omidubicel could potentially provide a superior graft for unrelated donor transplantation in patients who do not have a matched adult donor option in a timely manner, thereby addressing a critical unmet need in the treatment of hematological malignancies.

Gamida Cell, Ltd. is developing omidubicel for the treatment of hematological malignancies in adults and pediatrics. The non-proprietary name omidubicel is applied throughout this report, however omidubicel was previously referred to as NiCord.

The purpose of this pivotal Phase III, controlled, open-label, multicenter, international, randomized study was to compare transplantation of omidubicel to transplantation of one or two unmanipulated, unrelated CBUs to characterize omidubicel's clinical efficacy and safety profiles. The study was conducted in patients (N= 125) with hematological malignancies for whom allogenic SCT is currently a recommended and potentially life-saving treatment, all with required disease features rendering them eligible for allogeneic transplantation.

The Sponsor has conducted several clinical studies with omidubicel as presented in Table 2, where overall results demonstrate favorable safety and efficacy profiles.

To address the limitations of umbilical CB as a graft source, the sponsor is developing omidubicel, a therapy comprising *ex vivo* expanded hematopoietic stem cells and differentiated immune cells. Omidubicel is being developed to improve the HSCT options available to patients and is intended to serve as a graft source for the treatment of serious and life-threatening hematological malignancies.

Specifically, omidubicel comprises cord blood-derived allogeneic stem and progenitor cells expanded *ex vivo* from an entire CBU by cytokines (stem cell factor, thrombopoietin, Flt3-ligand, and interleukin-6), along with nicotinamide (NAM). The cells produced following a 3- week expansion process are myeloid cell subsets at different stages of maturation (such as CD15+, CD14+ and CD11+ cells) alongside CD34+ and CD133+ progenitor cells and CD133+/CD38- early progenitors, which are less differentiated. CD34+ and CD133+ are specific surface markers characterizing hematopoietic stem/progenitor cells with high self-renewal potential. Both of these markers characterize hematopoietic stem cells which can support short and long-term engraftment and are strongly associated with survival following stem cell transplantation in humans. Preclinical models of stem cell engraftment evaluated the potential of CD34+ cells to home to the bone marrow (BM) and differentiate into mature hematopoietic cells. NAM was shown to enhance the migratory potential and increase the homing efficacy of *ex vivo* expanded CD34+ cells derived from CBU, demonstrating the potential efficacy of omidubicel in animal models (Peled, Shoham et al. 2012).

Table 2: Summary of Clinical Studies Conducted with Omidubicel

Study Number	ClinicalTrials.gov ID	Title	Countries	Patient Population	Phase	Patients Treated with Omidubicel	Treatment Description	Status
GC P#01.01.020 P0101	NCT01221857	Allogeneic Stem Cell Transplantation of omidubicel, in Combination with a Second, UCBU in Patients with Hematologic Malignancies	U.S.	Hematologic malignancies	I/Pilot	11	Omidubicel in combination with UCBU	Completed
GC P#03.01.020 P0301	NCT01816230	Allogeneic Stem Cell Transplantation of omidubicel in Patients with Hematological Malignancies	U.S., Spain, Italy, Netherlands, Singapore	Hematologic malignancies	I/II	36+2	Single unit omidubicel (36); 2 patients received omidubicel + UCBU	Completed
GC P#07.01.020 P0701	NCT04260698	An Open-Label Expanded Access Study of omidubicel, for Allogeneic Transplantation in Patients with Hematological Malignancies	U.S.	Hematologic malignancies	IIIb (Expanded access)	13	Single unit omidubicel	Ongoing
GC P#02.01.020 P0201	NCT01590628	Allogeneic Stem Cell Transplantation of omidubicel in Patients with Hemoglobinopathies	U.S.	Hemoglobinopathies	I/II	16	13 patients received omidubicel and UCBU; three patients received single unit omidubicel	Completed
GC P#01.01.030 P0113	NCT02504619	Allogeneic Stem Cell Transplantation of omidubicel in Patients with Hemoglobinopathies	U.S.	Hemoglobinopathies	I/Pilot	1	Single unit omidubicel	Completed
Protocol #17- H-0091 IND #17348 IST	NCT03173937	Umbilical CBT for Severe Aplastic Anemia and Hypo-plastic MDS using omidubicel	U.S.	Aplastic anemia	II	9	3 patients received omidubicel and haploidentical CD34+ cells; six patients received single unit omidubicel	Ongoing

Abbreviations: CBT: Cord blood transplantation; MDS: Myelodysplastic Syndrome; UCBU: Unmanipulated cord blood unit

8 STUDY OBJECTIVES

The overall study objective was to compare the safety and efficacy of omidubicel single *ex vivo* expanded CBU transplantation to unmanipulated CBU transplantation in patients with hematological malignancies following conditioning therapy.

The study objectives were selected to assess the hypothesis that omidubicel as a standalone graft will improve post-transplant outcomes compared to umbilical cord blood transplantation (CBT).

8.1 Primary Objective(s)

The primary objective was to assess the time to neutrophil engraftment following transplantation.

8.2 Secondary Objective(s)

The secondary objectives were to assess the following endpoints:

- Incidence of Grade 2/3 bacterial or invasive fungal infections by 100 Days following transplantation
- Days alive and out of hospital in the first 100 Days following transplantation
- Platelet engraftment by 42 Days following transplantation

Tertiary Endpoint:

- Non-relapse mortality by 210 Days following randomization

Exploratory Endpoints:

- Neutrophil engraftment by 16 Days following transplantation
- Time from transplantation to platelet engraftment
- Duration of primary hospitalization
- Non-relapse mortality by 130 Days and 15 Months following randomization
- Overall survival at 210 Days and 15 Months following randomization
- Disease-free survival at 15 Months following randomization
- Neutrophil engraftment by 42 Days following transplantation
- Acute GvHD Grade II-IV and Grade III-IV by 100 Days following transplantation
- Chronic GvHD (mild/moderate/severe) by 180 Days and one year following transplantation
- Secondary graft failure by one year following transplantation
- Grade 3 viral infections by 180 Days and one year following transplantation
- Safety and tolerability of omidubicel transplantation
- Relapse by 15 Months following randomization

- Relapse mortality by 15 Months following randomization
- Immune reconstitution at 28, 70, 100, 180, and 365 Days following transplantation
- Supplemental immune reconstitution assessments at a central laboratory (optional)
- Health-related quality of life
- Long-term clinical outcomes up to five years following transplantation (optional)

9 INVESTIGATIONAL PLAN

This study was conducted in accordance with Gamida Cell Protocol GC P#05.01.020 (P0501), "A Multicenter, Randomized, Phase III Registration Trial of Transplantation of omidubicel (NiCord®), *Ex Vivo* Expanded, Umbilical Cord Blood-derived, Stem and Progenitor Cells, versus Unmanipulated Umbilical Cord Blood for Patients with Hematological Malignancies," Amendment VI, dated 22 January 2019. Enrollment into this study began under Amendment II of the protocol dated 27 October 2016. Details on protocol amendments are provided in Section 9.8.1.

Details of the study plan and data collection are provided in the protocol and protocol amendments in Appendix 16.1.1. Samples of the electronic Case Report Forms (eCRF) for the study are provided in Appendix 16.1.2, and a copy of the Statistical Analysis Plan (SAP) is provided in Appendix 16.1.9.

9.1 Overall Study Design and Plan

This study was designed as an open-label, controlled, multicenter, Phase III, randomized study of transplantation of omidubicel versus unmanipulated CBU in patients with hematological malignancies.

The study was planned to randomize 120 patients to transplantation of omidubicel or unmanipulated CBU in a 1:1 ratio. For additional discussion of statistical methods, see Section 9.7.

Study endpoints are detailed in Section 8.

9.2 Discussion of Study Design

The study schema outlining the overall study design is presented in Figure 1. This study comprised patients aged 12-65 years old with hematological malignancies and no available matched sibling or matched unrelated adult donor who were eligible at multiple international centers between December 2016 and December 2019. Eligibility required the availability of a CBU that met specific requirements for HLA matching, as well as CD34+ cell count, TNC cell count, and TNC cell dose. Detailed patient and CBU eligibility are given in Sections 9.3.1, 9.3.2, and 9.4.4. Additionally, if randomized to the control arm, specifications for use of a second CBU were outlined in the protocol depending on HLA, TNC dose, and CD34+ cell dose of the initial CBU selected. The investigator was required to make the determination prior to randomization if using one or two CBUs if randomized to the control arm.

Once confirmed by the PI the patient and CBU(s) were eligible per protocol, the patient was randomized in the database to either omidubicel or unmanipulated CBU. Following randomization, the CBU(s) were shipped accordingly:

- For patients randomized to omidubicel, the CBU was directly shipped from the Cord Blood Bank (CBB) to the production site to begin manufacturing (approximately 21 days). Timelines for shipment of omidubicel from the production site to the center prior to transplant were coordinated by the Study Logistics Manager (SLM) and the site staff.

- For patients randomized to unmanipulated CBU, the center was responsible to coordinate shipment of the CBU(s) from the CBB to the center prior to transplant.

Designated conditioning regimens were used, including total body irradiation (TBI)/Flu/Thiotepa, TBI/Flu/±Cy and Thiotepa/Bu/Flu with specifications for each outlined in Section 9.4.1.1. Centers were required to commit to using the same conditioning regimen for all patients at the transplant center or according to primary diagnosis/age group.

GvHD prophylaxis comprised tacrolimus or cyclosporine, and mycophenolate mofetil, with centers required to commit to using the same calcineurin inhibitor for all patients at the transplant center starting three days before transplantation. Mycophenolate Mofetil and tacrolimus/cyclosporine were continued for a minimum of 60 days and 100 days following transplantation, respectively.

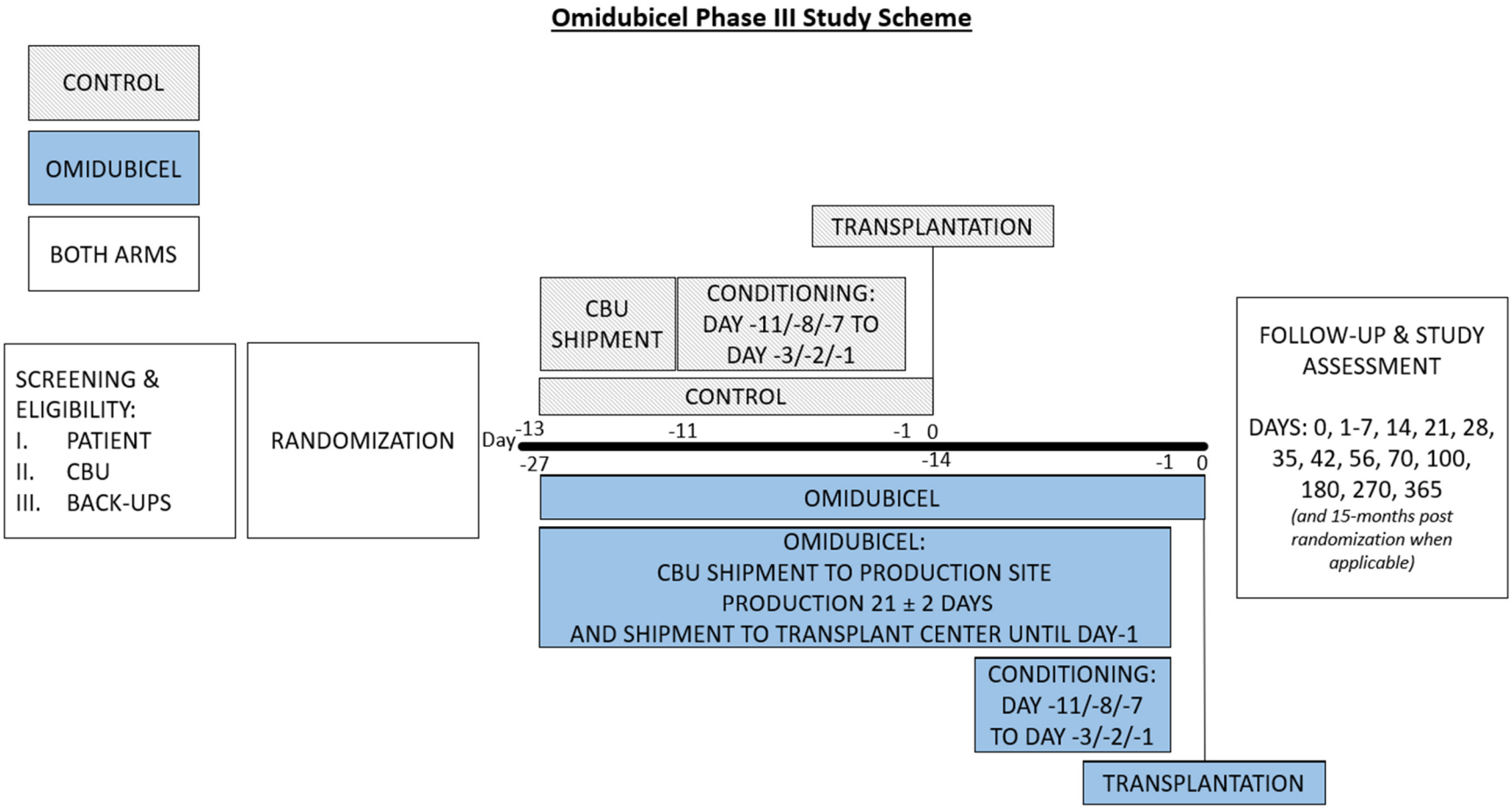
Prior to the start of the conditioning regimen, the center was required to confirm the patient remained suitable for transplant according to site practice. All patients received premedication prior to infusion which included diphenhydramine (or Dexchlorpheniramine), Hydrocortisone, and acetaminophen/Paracetamol. Preparation and infusion of the study product was as follows:

- For patients randomized to omidubicel, the study product was thawed and diluted with the infusion solution according to the Sponsor SOPs. Infusion of omidubicel was performed according to the protocol: The CF was infused first, followed immediately (up to 1 hour) by the infusion of the NF.
- For patients randomized to unmanipulated CBU, preparation and infusion of the CBU(s) was performed according to site practice.

All patients who were transplanted within 90 days post-randomization were followed weekly through Day 42 post-transplant and then at the designated study visits through Day 365 with final contact at 15 Months post-randomization for survival and relapse status as detailed in Table 7.

Patients who failed to receive a transplant within 90 days post-randomization (with any stem cell source) were followed for safety assessments at Days 90, 130, 210, and 365 post-randomization with final contact at Day 457 (15 Months) post-randomization for survival and relapse status (Figure 1).

Figure 1: Study Schema



9.3 Selection of Study Population

9.3.1 Inclusion Criteria

1. Patients must have been 12-65 years of age at the time of randomization
2. Patients with one of the following hematological malignancies:
   a. ALL at one of the following stages:
      i. High-risk first complete morphologic remission (CR1), defined as one or more of the following:
         1. The presence of adverse cytogenetics or adverse molecular changes. Examples of adverse cytogenetics are t(4;11), t(9;22), t(1;19), MLL rearrangements t(11q23), or severe hypodiploid ALL
         2. Extreme leukocytosis at diagnosis (WBC > 30,000/μL for B-ALL or > 100,000/μL for T-ALL)
         3. Failure to achieve complete morphologic remission after first induction therapy
         4. Evidence of minimal residual disease (MRD) at screening by flow cytometry or molecular testing
         5. Evidence of slow response to induction therapy, such as peripheral blood leukemic blasts one week after start of induction, or > 10% leukemic blasts in BM two weeks after start of induction
         6. Age older than 30 years at diagnosis
      ii. Second or subsequent complete morphologic remission
   b. AML at one of the following stages:
      i. First complete morphologic remission (CR1) that was NOT considered as favorable risk
      Favorable risk was defined as having one or more of the following at diagnosis and absence of MRD at screening:
         1. t(8,21) without cKIT mutation
         2. inv(16) or t(16;16) without cKIT mutation
         3. Normal karyotype with mutated NPM1 and no FLT-3 Internal Tandem Duplication
         4. Normal karyotype with double mutated CEBPA
         5. APL in first or second molecular remission at end of consolidation
      ii. Patients in CR1 with one or more of the favorable risk criteria but with additional high-risk features may have been considered eligible upon consultation with the study chairs.
      iii. Second or subsequent remission.
   c. Chronic myelogenous leukemia (CML) at one of the following phases:
      i. Chronic phase with one or more of the following characteristics:

1. Failure to achieve a primary hematologic or cytogenetic response to either nilotinib or dasatinib (following European LeukemiaNet timelines summarized in Protocol Appendix H [Appendix 16.1.1])
2. Intolerance to/failure of two tyrosine kinase inhibitors (TKI)
3. Any T315I mutation
4. Prior blast crisis

ii. Accelerated phase with one or more of the following characteristics:
1. Newly diagnosed patients who did not achieve an optimal response to TKIs as outlined in the European LeukemiaNet timelines summarized in Protocol Appendix H (Appendix 16.1.1)
2. TKI-treated patients who progressed from chronic phase

iii. Prior blast crisis (myeloid or lymphoid) that was currently in chronic phase or in complete morphologic or molecular remission

d. CMMoL or myelodysplastic syndrome (MDS)/CMMoL overlap with spleen size < 13 cm

e. MDS with history of one or more of the following:
i. International Prognostic Scoring System (IPSS) risk category of INT- 1 or greater. MDS patients categorized as INT-1 on primary presentation must have had life-threatening neutropenia (ANC < 0.5×10^9/L) or thrombocytopenia (platelets < 30×10^9/L).
ii. Revised International Prognostic Scoring System (IPSS-R) risk category of intermediate or greater

f. Biphenotypic/undifferentiated/Prolymphocytic/Dendritic Cell Leukemias and Natural Killer Cell Malignancies in first or subsequent CR, adult T-cell leukemia/lymphoma in first or subsequent CR

g. Lymphoma, meeting one or more of the following criteria:
i. Burkitt's lymphoma in second or subsequent CR
OR
ii. High-risk lymphomas in first CR, including enteropathy-associated T-cell lymphoma and hepatosplenic γδ T-cell lymphoma
OR
iii. Chemotherapy-sensitive (defined as at least stable disease) lymphomas that had failed at least one prior regimen of multi-agent chemotherapy and were not candidates for an autologous transplant.
(Patients with CLL were not eligible regardless of disease status).

3. CBU criteria as described in Section 9.4.4 and summarized below.
a. HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. High-resolution matching was required for HLA class II. At least one allele match at DRB1 was required.
b. The CBU intended for expansion was required to contain a pre-cryopreserved (post-processing) total CD34+ cell count of at least 8×10^6, as well as a pre-

cryopreserved (post-processing) total nucleated cell count of at least 1.8×10^9, and a total nucleated cell dose of at least 1.5×10^7 TNC/kg body weight

c. If the CBU was HLA-matched at 5-6/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $< 2.5 \times 10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.2 \times 10^5$ CD34+ cells/kg, a second CBU was required to be added for the control arm, as a double CBT.

d. If the CBU was HLA-matched at 4/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $< 3.5 \times 10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.7 \times 10^5$ CD34+ cells/kg, a second CBU was required to be added for the control arm, as a double CBT.

e. In case of double CBT in the control arm: The two CBUs were required to have a combined pre-cryopreserved (post-processing) total nucleated cell dose of $\geq 3 \times 10^7$ TNC/kg.

4. Patients who were to starting conditioning prior to omidubicel release for infusion (i.e., omidubicel arrival on site in adequate condition) must have had an additional partially HLA-matched CBU reserved as a backup to the omidubicel arm in case of production failure. The backup CBU must have been HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. A second backup CBU was recommended to be added in the below cases:

   a. If the backup CBU was HLA-matched at 5 or 6/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $< 2.5 \times 10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.2 \times 10^5$ CD34+ cells/kg.

   b. If the backup CBU was HLA-matched at 4/6, and contained a pre- cryopreserved (post-processing) total nucleated cell dose of $< 3.5 \times 10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.7 \times 10^5$ CD34+ cells/kg.

      In case of two backup CBUs, the second backup CBU had to also be HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. The backup CBUs were recommended to have a combined pre-cryopreserved (post-processing) total nucleated cell dose of at least 3×10^7 TNC/kg.

5. Patient's Performance score ≥ 70% by Karnofsky or Lansky
6. Patient had sufficient physiologic reserves including:
   a. Cardiac: Left ventricular ejection fraction (LVEF) of ≥ 40% by echocardiogram, radionuclide scan or cardiac MRI, or left ventricular shortening fraction ≥ 29%.
   b. Pulmonary function tests (prior to treatment with bronchodilators) demonstrating FVC and FEV1 of > 50% of predicted for age and (carbon monoxide diffusing capacity) cDLCO > 50% of predicted for patients in whom pulmonary function testing could have been performed (If PFT testing included the use of bronchodilators, then the baseline results during testing prior to the administration of any medications should have been used when determining eligibility).
   c. Renal: Creatinine clearance test (by Cockcroft-Gault equation) ≥ 60 mL/min

d. Hepatic: Serum Bilirubin < 2.0 mg/dL; Hepatic transaminases (ALT and AST) < 3 x upper limit of normal range

7. Females of childbearing potential, defined as any female who had experienced menarche and was not postmenopausal (defined as not having had a menstrual period for at least 24 months) or permanently sterilized (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy), agreed to use an appropriate method of contraception from at least 7 days prior to conditioning regimen therapy until completion of follow-up procedures. An appropriate method of contraception was defined as one that results in a low failure rate (i.e., less than 1 percent per year) when used consistently and correctly, such as implants, injectables, combined oral contraceptives, intrauterine contraceptive devices (IUDs), true sexual abstinence (when this was in line with the preferred and usual lifestyle of the patient), or a vasectomized partner.
8. Patient (or legal guardian) signed the written informed consent after being aware of the nature of the patient's disease and willingly consented to the treatment program after being informed of alternative treatments, potential risks, benefits, and discomforts.

9.3.2 Exclusion Criteria

1. MDS or CML with "marked" or "3+" fibrosis
2. Chronic lymphocytic leukemia (CLL)
3. Fewer than 21 days had elapsed since initiation of the patient's last chemotherapy cycle and the initiation of the stem cell transplant (SCT) preparative regimen (radiotherapy, intrathecal agents, hydroxyurea, TKI, hypomethylating agents, rituximab, blinatumomab and lenalidomide were not considered chemotherapy)
4. Persistent clinically significant toxicities that, in the investigator's opinion, made the patient unsuitable for transplant
5. Evidence of donor specific anti-HLA antibodies to the selected CBU intended for expansion (MFI> 3000 to HLA-A, B, C, or DRB1)
6. Evidence of HIV infection or HIV positive serology
7. Evidence of active Hepatitis B or Hepatitis C as determined by serology or polymerase chain reaction (PCR)
8. Pregnancy, as indicated by a positive serum or urine human chorionic gonadotrophin (HCG) test, or lactation
9. Active malignancy other than that for which the CBT was being performed within 12 months of enrollment. Fully resected cutaneous squamous cell or basal cell carcinoma or cervical carcinoma in situ within 12 months of enrollment were permitted.
10. Evidence of uncontrolled bacterial, fungal or viral infections or severe concomitant diseases, which in the judgment of the Principal investigator indicated that the patient could not tolerate transplantation
11. Patients with presence of leukemic blasts in the central nervous system (CNS)
12. Patients with an 8/8 allele level HLA-matched and readily available related or unrelated donor (whose stem cells could have been collected in a timely manner

without jeopardizing recipient outcome). Patients who had haploidentical related donors or syngeneic donors were excluded

13. Prior allogeneic hematopoietic SCT
14. Allergy to bovine products, gentamicin, or to any other product that may have interfered with the treatment
15. Psychologically incapable of undergoing bone marrow transplant (BMT) with associated strict isolation or documented history of medical non-compliance and/or psychiatric illness and/or social situations that would have limited compliance with study requirements
16. Enrolled in another interventional clinical trial or received an investigational treatment within 30 days prior to the anticipated date of randomization, unless documented approval obtained from Sponsor prior to randomization

9.3.3 Removal of Patients from Dosing or Assessment

Patients could have been discontinued from dosing or from the study for any of the following reasons

- Patient withdrew consent
- Sponsor requested patient to be withdrawn
- Request of primary care physician or investigator

Reasons for withdrawal of the patient prior to end of study were stated in the CRF and in the site source documentation for all study patients who were enrolled in the study, including patients who were screened and assigned a screening number but were not randomized. Patients were defined as screening failures when withdrawn from the study before randomization.

Patients who were randomized but did not receive a SCT within 90 days post-randomization are part of the ITT analysis and were to be followed for Grade 2 and 3 infections, survival status, relapse, and Health-Related Quality of Life (HRQoL) at 90, 130, 210, and 365 Days post-randomization with an additional assessment of survival and relapse status at 15 Months post-randomization. All other assessments were not required for these patients unless they received a SCT within 90 days post-randomization, at which point they would be followed according to the protocol-specified scheduled visits post-transplant. For early withdrawal patients who withdrew or were withdrawn from the study post-transplant, any assessments due at the time of withdrawal were requested.

Patients who experienced graft failure or relapse post-transplant continued to be followed according to the study visit schedule for hospitalizations, Grade 2 and 3 infections, relapse (except patients with prior post-transplant relapse), graft failure (except patients with prior post-transplant graft failure), survival status, and HRQoL. For these patients, all SAEs were reported until at least 30 days post-transplant. After Day 30 post-transplant and following date of relapse or graft failure, only SAEs resulting in death or with suspected causal relationship to the infused product were reported. No other study-related assessments were required for these patients after the date of graft failure or relapse.

9.4 Study Treatment

9.4.1 Treatments Administered and Supportive Care

Patients (N=125) were randomized in a 1:1 ratio and received either omidubicel or unmanipulated CBU transplantation. Patients were randomized to one of two treatment arms:

- Omidubicel
- Unmanipulated CBU

9.4.1.1 Conditioning Regimen

All patients received one of three conditioning regimens as outlined in Table 3, Table 4, and Table 5. Each transplant center was required to commit to use the same conditioning regimen for all patients transplanted at their center or according to primary diagnosis/age group. The intended practice was documented prospectively for the transplant center. In unique cases where the use of a different conditioning regimen was deemed to be in a patient's best interest, approval from one of the study chairs was required prior to use of the different regimen. Prior to randomization, the investigator determined the conditioning regimen intended for use in the transplantation.

Table 3: Conditioning Regimen A.1

Study Day / Treatment	-11	-10	-9	-8	-7	-6-	-5	-4	-3	-2	-1	0
TBI 1350 cGy in 8 or 9 fractions[a]			×2 or ×1 or ×0	×2	×2	×2	×0 or ×1 or ×2				REST	Infusion of omidubicel or unmanipulated CBU/s
Fludarabine[b] 40 mg/m^2 IV							×	×	×	×		
Thiotepa[a] 5 mg/kg IV	×	×										

Data Source: Protocol GC P#05.01.020 (Appendix 16.1.1)
[a] Or TBI 1200 cGy, administered as per institutional practice
[b] Adjusted body weight
Abbreviations: TBI: Total body irradiation; CBU: Cord blood unit

Table 4: Conditioning Regimen A.2

Treatment \ Study Day	-8	-7	-6	-5	-4	-3	-2	-1	0
TBI 1320 cGy in eight fractions[a]				REST[b]	×2	×2	×2	×2	Infusion of omidubicel or UCBU/s
Fludarabine 25 mg/m^2 IV	×	×	×						
Cyclophosphamide[c] 60 mg/kg IV	×	×							

Data Source: Protocol GC P#05.01.020 (Appendix 16.1.1)

[a] Or TBI 1200 cGy, administered as per institutional practice

[b] A day of rest may be included between the last dose of fludarabine and the start of TBI (as shown above). Alternatively, the day of rest may be moved to Day -1 without any rest between fludarabine and TBI (TBI on Day -5, -4, -3, -2) or the day of rest may be omitted altogether (Cyclophosphamide on Day -7 and -6 and fludarabine on Day -7, -6 and -5)

[c] Adjusted body weight

Abbreviations: TBI: Total body irradiation; CBU: Cord blood unit; UCBU: Unmanipulated cord blood unit

Table 5: Conditioning Regimen B

Treatment \ Study Day	-7	-6	-5	-4	-3	-2	-1	0
Thiotepa[a] 5 mg/kg IV	×	×				REST		Infusion of omidubicel or UCBU/s
Busulfan[a] 3.2 mg/kg IV or weight-based dosing + TDM[b]		×[c]	×	×	×			
Fludarabine[a] 50 mg/m^2 IV			×	×	×			

Data Source: Protocol GC P#05.01.020 (Appendix 16.1.1)

[a] Adjusted body weight

[b] TDM= therapeutic drug monitoring: aiming for cumulative target AUC = 75 mg*h/L. Busulfan levels after 1st dose will be measured at 5 min, 1h, 2h and 4h after end of Bu infusion and AUC will be calculated based on previously described population PK model (2)

[c] Can be added as per institutional practice

Abbreviations: AUC: Area under the curve; IV: Intravenous PK: Pharmacokinetic; UCBU: Unmanipulated cord blood unit.

9.4.1.2 GvHD Prophylaxis Medications

All patients received GvHD prophylaxis with two drugs as follows:

Calcineurin inhibitor (Tacrolimus or Cyclosporine)

Each transplant center had to commit to use the same calcineurin inhibitor (tacrolimus or cyclosporine) for all patients transplanted at their center. In unique cases where the use of a different calcineurin inhibitor was deemed to be in the patient's best interest, approval from the study chairs must have been obtained prior to use of the different calcineurin inhibitor. Prior to randomization, the investigator had to decide and document the GvHD prophylaxis intended to be used for transplantation.

Tacrolimus or cyclosporine from Day -3 to at least Day +100.

- Recommended target tacrolimus trough blood levels of 5-15 ng/mL.
- If administering via continuous IV infusion, it was recommended to target cyclosporine trough levels of 200-400 ng/mL by TDX method (or equivalent level for other CSA testing methods). For intermittent dosing, it was recommended to target

cyclosporine trough levels of 150-400 ng/mL by TDX method (or equivalent level for other CSA testing methods).
- In the event of toxicity, suspected relapse, or the development/worsening of GvHD, dosing may have been adjusted per institutional standard practice or a different drug may have been substituted. In the absence of actual toxicity, calcineurin inhibitor taper could have begun at Day +100 at the earliest, at the discretion of the managing physician, with the goal for discontinuation at Day 180-200.

Mycophenolate Mofetil (MMF)

Mycophenolate Mofetil (MMF) (or Mycophenolate Sodium) was to be given at a dose of 15 mg/kg TID (based upon actual body weight [ABW]) with the maximum total daily dose not to exceed 3 g (IV or PO rounded to the nearest capsule size) beginning Day -3 to at least Day +60. In the event of toxicity or suspected relapse, dosing may have been adjusted per institutional standard practice or a different drug may have been substituted.

9.4.1.3 Infusion Support

All patients received the following medications 30-60 mins prior to omidubicel or unmanipulated CBU infusion.

- Diphenhydramine 50 mg IV or PO (or 0.5 mg/kg up to a maximum of 50 mg) or Dexchlorpheniramine 10 mg IV
- Hydrocortisone 50 mg IV (or 0.5 mg/kg up to a maximum of 50 mg)
- Acetaminophen/Paracetamol 500-1000 mg IV or PO (or 10 mg/kg up to a maximum of 1000 mg)

Changes to the above medications for infusion support were allowed but had to be approved by the Sponsor prior to transplantation.

Methylprednisolone should not have been used in conjunction with standard delivery of omidubicel or unmanipulated CBU to the patient. Management of infusion reactions during and post-transplant was at the discretion of the managing physician.

9.4.1.4 Supportive Cytokine Therapy

Granulocyte colony-stimulating factor (G-CSF) (e.g., Filgrastim, Neupogen, Granix) therapy was started on Day +1 at a dose of 5 μg/kg/day (rounded to nearest vial size) given IV or SC and continued through the second day of ANC > 1,000/μL for two consecutive days.

9.4.1.5 Infection Prophylaxis and Surveillance

Unless otherwise specified, institutional guidelines were to be followed to provide prophylaxis for infections. In general, each transplant center should have used the same anti-microbial prophylaxis regimens for all patients transplanted at their center, apart from unique cases where the use of a different anti-microbial agent was deemed to be in the patient's best interest. Strict guidelines for hygiene and care were to be applied. Before starting the pre-transplant conditioning, there should have been no uncontrolled mucosal or cutaneous infections. Oral Candida prevention should have been vigorously pursued.

All patients were to be nursed in a single room during neutropenia and should preferably have been nursed in a single room during all admissions. All visitors were to be free of active infections.

Anti-bacterial prophylaxis was required, with a recommendation for ciprofloxacin 500 mg PO BID on Days 0-100. For PCP prophylaxis, trimethoprim-sulfamethoxazole or an equivalent drug was to be administered after engraftment. Anti-viral and anti-fungal prophylaxis was recommended.

All recipients were to be tested for CMV (using the PCR method) at least once during the conditioning period at the weekly protocol-specified visits (Appendix 16.1.1) up through Day 42 and then on Day 56, 70 and Day 100 or more frequently as clinically indicated.

Quantitative HHV6 DNA assessment by PCR was to be tested at weekly protocol-specified visits after transplantation until absolute neutrophil count (ANC) > 500 cells/µL.

Quantitative Epstein-Barr virus (EBV) viral load assessment by PCR was to be tested at protocol-specified visits on Days 21, 56, and 100 post-transplant or more frequently as clinically indicated and at protocol-specified visits on Days 180, 270, and 365 post-transplant if the patient was still on immunosuppression.

As standard treatment practices differ between institutions and vary by patient circumstance, treatment of infections was according to the managing physician and per institutional practice.

9.4.1.6 Blood Products

Platelet counts were to be maintained at > 10,000/µL after transplantation by transfusion of platelets. When available, single donor platelets were to be used.

Transfusions of packed red blood cells (RBC) were indicated for the management of symptomatic anemia per institutional guidelines. In the absence of symptoms, RBC transfusions were to be considered to maintain hemoglobin > 7 g/dL.

All blood products (except omidubicel or any other stem cell grafts administered) were to be irradiated to at least 2500 cGy before administration to transplant recipients to reduce the risk of developing third-party graft-versus-host disease (GvHD).

9.4.2 Identity of the Investigational Product

Omidubicel is a cryopreserved cell-based product of allogeneic, *ex vivo* expanded, umbilical cord blood-derived, hematopoietic CD34+ progenitor cells (omidubicel CF) and the non-expanded cell fraction of the same CBU (omidubicel NF) consisting of mature myeloid and lymphoid cells.

Briefly, production of omidubicel involves *ex vivo* culture of purified CD133+ cells derived from a single CBU for 21 (±2) days in the presence of the cytokines SCF, TPO, IL6 and Flt3-L, 50 ng/mL each, 2.5 mM NAM, FBS and culture medium.

On Day 21 (±2) the cells are washed twice and cryopreserved in CryoStor®CS10. On the day of transplantation, the cells are thawed and reconstituted by a 1:5 dilution with the infusion solution. Harvest can be carried out from Day 19 and up to Day 23 if the patient's clinical condition or logistic considerations require an earlier transplantation date or a delay.

9.4.3 Method of Assigning Patients to Treatment Groups

The study randomized subjects 1:1 to omidubicel or unmanipulated CBU using the enrollment module of the Advantage eClinical® system. The randomization was designed to provide an approximately balanced allocation to the treatment groups during the study. The study used a form of randomization known as minimization that is designed to ensure that the treatment groups were well-balanced with respect to selected factors of prognostic importance. The factors in the minimization algorithm included the following: treatment center, disease risk group, age group, and intent to perform single vs. double cord transplant in the control arm. A random element was included in the assignment, whereby when the minimization algorithm indicated a preference to allocate a specific treatment, say omidubicel, then that treatment was allocated with probability 0.9. If the algorithm indicated no preference, then a probability of 0.5 was used.

9.4.4 Selection of Doses in the Study

With regard to HLA matching, all CBUs, whether intended for treatment or as backup CBUs, were required to be HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. Low level DNA/molecular matching was sufficient for HLA class I; however, serologic matching could also be used. High-resolution matching was required for HLA class II. At least one allele match at DRB1 was required.

The CBU intended for expansion was required to contain a pre-cryopreserved (post-processing) total CD34+ cell count of at least 8×10^6, as well as a pre-cryopreserved (post-processing) total nucleated cell count of at least 1.8×10^9, and a total nucleated cell dose of at least 1.5×10^7 TNC/kg body weight, a dose predicted to be sufficient in size to provide robust and sustained engraftment, based on the clinical experience with omidubicel.

This CBU was designed to be used for the omidubicel arm or for the control arm in case of either single or double unmanipulated CBT:

- In case this CBU was HLA-matched at 5-6/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $< 2.5 \times 10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.2 \times 10^5$ CD34+ cells/kg, a second CBU was required to be added for the control arm, as a double CBT.
- In case this CBU was HLA-matched at 4/6 and contained a pre-cryopreserved (post-processing) total nucleated cell dose of $< 3.5 \times 10^7$ TNC/kg, OR a pre-cryopreserved (post-processing) CD34+ cell dose of $< 1.7 \times 10^5$ CD34+ cells/kg, a second CBU was required to be added for the control arm, as a double CBT.

The determination of using a single or double CBU for transplant was required to be made by the investigator prior to randomization.

In case of double CBT: The two CBUs were required to have a combined pre-cryopreserved (post-processing) total nucleated cell dose of $\geq 3 \times 10^7$ TNC/kg.

The criteria were intended to assure that CBUs of sufficient cell dose and CD34+ cell dose were used for both the treatment and the control arms, and reflect the published cut-offs for CBT, since successful CBT is dependent on sufficient CBU total nucleated cell dose, and

specifically sufficient CD34+ cell dose. The criteria for CBU selection for the control group were adapted from the formal guidelines for CBT (Apperley 2012).

Following production, omidubicel CF was required to contain > 8.0×10^8 total nucleated cells and > 5.6×10^7 CD34+ cells while omidubicel NF was required to contain > 4.0×10^8 TNC and > 2.4×10^7 CD3+ cells.

9.4.5 Selection and Timing of Dose for Each Patient

Decisions on the selection of CBUs are never arbitrary, but rather are based on specific histocompatibility data, cell dose, availability, and in some cases, the source of the CBU. However, there is no clear consensus or evidence-based algorithm as to the hierarchy of these factors. Thus, some physicians believe cell dose is of greatest importance, some examine CD34+ dose, and others prioritize HLA matching. For this reason, the protocol did not specify prioritization rules when more than one eligible CBU was identified.

Omidubicel is administered as a single, one-time infusion of two separate fractions; the Cultured Fraction (CF) and the Non-Cultured Fraction (NF). The date and time of the transplant was determined by each individual investigator based on patient needs, availability of the transplant product, and coordination with the site's transplant staff. The day of transplant must follow the completion of a protocol-specified conditioning regimen.

9.4.6 Blinding

This was an open-label study. To minimize potential bias, the sponsor and the principal statistician did not have access to the aggregate clinical trial data and were blinded from all interim analyses provided to the DMC. A summary of blinding procedures can be found in Appendix 16.1.9.

9.4.7 Prior and Concomitant Therapy

All medications taken by/given to the patient as a treatment for the primary and concomitant diseases within 30 days prior to screening were recorded in the patient files. All chemotherapy and radiotherapy courses administered to patients as prior treatment for hematological malignancy were recorded in the CRF (including treatment regimen, number of cycles, and dates).

The following concomitant medications were prohibited to be administered post-transplant:

- Any cytokines except G-CSF should not have been used (including IL-2 or others, unless approved by Sponsor).
- The use of Bactrim (sulfamethoxazole and trimethoprim) or methotrexate was discouraged on or after Day -2 until the time of engraftment as it could have delayed engraftment and was reserved only for cases where it was assessed to be essential and superior to all alternative medications.
- Maintenance therapies (e.g., TKIs, hypomethylating agents, antibodies) should not have been given within the first 100 Days post-transplant unless the platelet count was > 50×10^9/L with no platelet transfusions in the preceding seven days.

- Unless approved by the Sponsor, investigational agents should not have been administered from 30 days prior to randomization until the end of study follow-up for all patients randomized.

9.4.8 Treatment Compliance

Each dose of study product was administered by a member of the clinical research team who was qualified and licensed to administer the study product. Administration details, including date and time, were entered into the eCRF.

9.5 Efficacy and Safety Measurements

9.5.1 Efficacy Measurements

Efficacy measurements included the assessment of the primary endpoint, comparing time from transplant to neutrophil engraftment between patients allocated to receive omidubicel transplantation and those allocated to receive unmanipulated CBU transplantation. Definitions of all efficacy endpoints are included in Section 9.5.3 and further described along with corresponding results in Section 11.

9.5.2 Safety Measurements

Table 8 summarizes the schedule of safety assessments, which included monitoring AEs, concomitant medication(s), clinical laboratory analyses, vital sign measurements, and physical examinations. Study physicians authorized to make medical diagnoses were responsible for all study-related medical decisions.

The investigator and/or study personnel were to enquire about the occurrence of AEs at every visit, after the subject had the opportunity to spontaneously mention any problems. All AEs were to be recorded in the source documents with sufficient detail to allow for grading per CTCAE v4.03 and reported on the appropriate CRF page. All reported AEs and Serious Adverse Events (SAEs) were to be followed and recorded until resolution with or without sequelae, until the condition stabilized (the investigator did not expect any further improvement or worsening of the event), until an outcome was reached or the event was otherwise explained, or until there was agreement between the investigator and Sponsor that additional follow-up was not warranted. The investigator was to ensure that follow-up included any supplemental investigations as indicated to elucidate the nature and/or causality of the AE/SAE. This may have included additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals. Where appropriate, medical tests and examinations were to be performed to document resolution of the event(s). Additional follow-up information, if required, or available, was to be reported in the same timelines as initial information.

All laboratory measurements were to be evaluated for abnormalities. Since patients with severe hematologic malignancies undergoing myeloablative conditioning followed by allogeneic SCT are known to experience a broad spectrum of different laboratory abnormalities, an abnormal laboratory value was to be interpreted primarily in the context of the disease or the condition leading to it. The latter (instead of the laboratory abnormality itself) was reported as the adverse event and graded, whenever possible. A laboratory adverse event (i.e., a laboratory abnormality not associated with any particular clinical findings (e.g.,

symptoms, signs)) was to be reported when judged clinically significant by the investigator. An abnormal laboratory finding was not by itself considered to be an AE or SAE unless the investigator considered the abnormal finding to be of clinical significance.

Safety data was required to be reported from the time of consent through the end of study follow-up as summarized in Table 6.

Table 6: Safety Data Reporting for Transplanted Patients

From the Time of Consent	From the Time of Randomization	During Conditioning up to Start of Omidubicel or CBU Infusion	During Omidubicel or CBU Infusion through 24 hours Post Omidubicel or CBU Infusion	> 24 hours Post Omidubicel or CBU Infusion through Day 42	Day 43 through Day 365[a]
		Complete a Toxicity form with the highest grade of all common[*] AEs	Complete a Toxicity form with the highest grade of all common[*] AEs [#] All uncommon non-serious AEs must be listed individually on the AE Log form[#]	Complete a weekly Toxicity form with the highest grade of all common[*] AEs during that week[#] All uncommon non-SAEs must be listed individually on the AE Log form	
	Infection form and/or Death form is required when applicable. For infections, all Grade 2-3 infections post-randomization and all treated Grade 1 infections after the start of conditioning must be reported.				
Any event[b] that also meets the definition of an SAE requires submission of SAE summary forms. If the SAE is unexpected and associated with omidubicel, then an expedited report must be submitted. Any graft failure event (primary or secondary) or disease progression/relapse event should be reported as an SAE					
		A Hospitalization form required if applicable			
				Scheduled GvHD data collection at every visit on either the Acute GvHD or the Follow-Up GvHD form.	

Data Source: Protocol Appendix C (Appendix 16.1.1)
[*] See Protocol Appendix D (Appendix 16.1.1) for a list of common adverse events
[#] With the exception of infections and GvHD symptoms which are reported on the Infection form and GvHD forms respectively.
[a] An additional assessment of survival and relapse status is required on or after month 15 post-randomization. Death and or Relapse forms are required during this time period as applicable. In the event of death, SAE forms are also required.
[b] After Day 30 post-transplant and following date of relapse or graft failure only SAEs resulting in death or suspected to be related to the infused product will be reported.
Abbreviations: AE: Adverse event; CBU: Cord blood unit; GvHD: Graft versus host disease; SAE: Serious adverse event

Beginning with randomization, all Grade 2/3 infections and any treated Grade 1 infection were to also be reported.

Beginning with conditioning, the set of anticipated AEs listed in Protocol Appendix D (Appendix 16.1.1) were to be reported as the highest Grade over a period of time. These were events that are anticipated to occur commonly in the treated patient population, and therefore were reported on a designated form that allowed selection from a pre-populated list of events and maximal grading over a defined interval of time. The specific time periods for anticipated event reporting were:

- During conditioning prior to transplant
- During or within 24 hours following administration of either omidubicel or unmanipulated CBU
- After 24 hours following administration of either omidubicel or unmanipulated CBU through Day 7
- Day 8 through Day 14
- Day 15 through Day 21
- Day 22 through Day 28
- Day 29 through Day 35
- Day 35 through Day 42

Following Day 42, Grade 3-5 anticipated events were reported individually, and Grade 1-2 anticipated events were not reported.

Unanticipated events, i.e. those not listed in Protocol Appendix D (Appendix 16.1.1), were reported individually from the start of either omidubicel or unmanipulated CBU infusion through Day 42. Following Day 42, Grade 3-5 unanticipated events were reported individually, and Grade 1-2 unanticipated events were not reported.

All SAEs regardless of grade were reported individually from the time of consent through completion of follow-up.

All AEs were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 23.

9.5.3 Definition of Terms

9.5.3.1 Date of Randomization

The date of randomization was defined as the date that the patient's treatment assignment was issued.

9.5.3.2 Date of Transplant

The date of transplant was defined as the first date of stem cell infusion following randomization, regardless of stem cell source.

9.5.3.3 Neutrophil Engraftment

Neutrophil engraftment was defined as achieving an ANC $\geq 0.5 \times 10^9$/L on three consecutive measurements on different days with subsequent donor chimerism (≤ 10% host cells by peripheral blood chimerism or BM chimerism if peripheral blood chimerism is not available) at any time on or after the day of engraftment up to the earlier of Day 100 post-transplant, date of relapse, date of secondary graft failure, or date of death. The first day of the three measurements was designated the day of neutrophil engraftment and must have occurred on or before 42 days post-transplant (and prior to infusion of any additional stem cell product).

Primary graft failure was defined as failure to achieve neutrophil engraftment by Day 42 as described above. Infusion of a second stem cell product on or prior to Day 42 was considered primary graft failure, with the following exception:

- Infusion of an additional stem cell product after documented neutrophil engraftment was considered secondary graft failure, even if it occurred on or prior to Day 42.

The date of primary graft failure was designated as Day 43 post-transplant.

Secondary graft failure comprised documented neutrophil engraftment, followed by severe neutropenia ($< 0.5 \times 10^9$/L for three or more consecutive laboratory values on separate days) with marrow cellularity < 5%, without subsequent improvement occurring either spontaneously or after growth factor treatment. Infusion of an additional stem cell product after documented neutrophil engraftment was considered secondary graft failure. The earlier of the first day of severe neutropenia, as defined above, or the date of additional stem cell infusion was designated the date of secondary graft failure.

9.5.3.4 Platelet Engraftment

Platelet engraftment was defined as the first day of a minimum of three consecutive measurements on different days such that the patient has achieved a platelet count $> 20 \times 10^9$/L with no platelet transfusions during the preceding seven days (counting day of engraftment as one of the preceding seven days). The first day of the three measurements was designated the day of platelet engraftment and had to occur prior to any infusion of a second stem cell product.

9.5.3.5 Grade 2/3 Bacterial Infections and Invasive Fungal Infections

Invasive fungal infection was defined as any Grade 3 fungal infection. See Protocol Appendix G (Appendix 16.1.1) for infection grading criteria.

9.5.3.6 Duration of Primary Hospitalization

Duration of primary hospitalization was defined as the total number of days from transplant to first discharge from the hospital. Patients transplanted as outpatients were assigned a duration of zero days.

9.5.3.7 Days Alive and out of Hospital

A day alive and out of hospital was defined as a full day (calendar day) in which the patient was alive and not hospitalized. Partial days alive and out of hospital, such as the day of admission, day of discharge and day of death, did not count as a day alive and out of hospital.

The day of transplant did not count as a day alive and out of hospital, regardless of whether the patient was treated as an inpatient or outpatient.

9.5.3.8 Overall Survival

Overall survival was defined as the time from the date of randomization to the time of death from any cause.

9.5.3.9 Disease Relapse

Relapse of Malignancy

Testing for recurrent malignancy in the blood, marrow or other sites was used to assess relapse after transplantation. For this study, relapse was defined by either morphological or by cytogenetic evidence of AML, ALL, CML, or MDS consistent with pre-transplant features.

Minimal Residual Disease

Minimal residual disease (MRD) was defined by the sole evidence of malignant cells by flow cytometry, or by fluorescent *in situ* hybridization (FISH), or by Southern blot or Western blot, or by PCR, or by other techniques, in the absence of morphological or cytogenetic evidence of disease in blood or marrow. Because the frequency of testing for MRD was highly variable among centers, and the sensitivity varied significantly between laboratory techniques, evidence of MRD alone was not sufficient to meet the definition of relapse in the context of this trial. However, MRD that progressed was considered as relapse and the date of relapse was the date of detection of MRD, as described below.

Acute Leukemia

Relapse could have been defined as any of the following. When more than one of these criteria applied, the date on which the first criteria was met was considered the date of relapse, unless MRD was previously detected, in which case the date of MRD detection was considered as the date of relapse:

- 5% blasts in the marrow, not attributed to other causes (e.g., BM regeneration).
- The appearance of new dysplastic changes within the BM, not attributed to other causes.
- Reappearance of leukemic blasts in the peripheral blood.
- Reappearance and progression of a previous cytogenetic or molecular marker of disease present prior to transplantation.
- The development of extramedullary leukemia or leukemic cells in the cerebrospinal fluid.
- Institution of any therapy in response to detection of MRD, including withdrawal of immunosuppressive therapy or the addition of TKI or hypomethylating agents, could be considered evidence of relapse regardless of whether the criteria described above were met.

Chronic Myelogenous Leukemia (CML)

If more than one of these criteria applied, the date on which the first criteria was met was considered the date of relapse, unless MRD was previously detected, in which case the date of MRD detection was the date of relapse.

Hematologic relapse could have been diagnosed when:

- Immature hematopoietic cells were persistently documented in the peripheral blood; or,
- There was myeloid hyperplasia in the BM in the presence of cytogenetic relapse.

Cytogenetic relapse could have been diagnosed when:

- 50% of the metaphases exhibited the characteristic (9;22) translocation with at least ten metaphases analyzed; or,
- At least one metaphase exhibited the (9;22) translocation on each of two separate consecutive examinations at least one month apart, regardless of number of metaphases analyzed. The date of the earliest test was considered the date of relapse.

MDS

Relapse could have been defined as any of the following. If more than one of these criteria applied, the date on which the first criteria was met as considered the date of relapse, unless MRD was previously detected, in which case the date of MRD detection was considered as the date of relapse:

- Satisfied the above criteria for evolution into acute leukemia; or,
- Reappearance of pre-transplant morphologic abnormalities, detected in two consecutive BM specimens obtained at least one month apart (the date of the earliest test was considered the date of relapse); or,
- Reappearance of pre-transplant cytogenetic abnormality in at least one metaphase on each of two separate consecutive examinations obtained at least one month apart, regardless of the number of metaphases analyzed.
- Institution of any therapy in response to detection of MRD, including withdrawal of immunosuppressive therapy or treatment with hypomethylating agents, could be considered evidence of relapse regardless of whether the criteria described above were met.

Lymphoma

Relapse could have been defined according to the following criteria:

- Appearance of any new lesion more than 1.5 cm in any axis during or at the end of therapy, even if other lesions are decreased in size. Increased fluorodeoxyglucose (FDG) uptake in a previously unaffected site was only considered relapsed or progressive disease after confirmation with other modalities. The therapeutic decision could not be made solely from the positron emission tomography (PET) scan without histologic confirmation.

- At least a 50% increase from nadir in the sum of the product diameters (SPD) of any previously involved nodes, or in a single involved node, or in the size of other lesions (eg splenic or hepatic nodules). To be considered progressive disease, a lymph node with a diameter of the short axis < 1.0 cm had to increase by $\geq 50\%$ to a size of 1.5×1.5 cm or > 1.5 cm in the long axis.
- Lesions were required to be PET positive if observed in a typical FDG-avid lymphoma or if the lesion was PET positive before therapy unless the lesion was too small to be detected with current PET systems (< 1.5 cm in its long axis by CT).
- Institution of any therapy to treat persistent, progressive, or relapsed disease, including withdrawal of immunosuppressive therapy or donor lymphocyte infusion (DLI), could be considered evidence of relapse/progression regardless of whether the criteria described above were met.

9.5.3.10 Disease-Free Survival

Disease-free survival was defined as the time from the date of randomization to the date of disease relapse or to the date of death from any cause, whichever occurred first.

9.5.3.11 Non-Relapse Mortality

Non-Relapse mortality was defined as any death not preceded by relapse.

9.5.3.12 Relapse Mortality

Relapse mortality was defined as any death preceded by relapse.

9.5.3.13 Acute GvHD

Acute GvHD was staged and graded using the Consensus Conference on Acute GvHD grading (Protocol Appendix B, Appendix 16.1.1) at every protocol-specified scheduled visit up to Day 180 post-transplant. The start date of GvHD was assigned as the visit number in which it was first diagnosed and is recorded separately for Grade II-IV GvHD and Grade III-IV GvHD.

9.5.3.14 Chronic GvHD

Chronic GvHD was assessed on the day of diagnosis, as well as on Day 100, 180, 270 and year one post-transplant, and classified as mild/moderate/severe according to the 2014 NIH Consensus Criteria (Protocol Appendix B, Appendix 16.1.1).

9.5.3.15 Immune Reconstitution

Immune reconstitution was assessed on Days 28, 70, 100, 180, and 365. Cellular immune recovery was assessed based on lymphocyte subset analysis to quantify the numbers and proportions of different lymphocyte subpopulations (CD3, CD4, CD8, CD19, CD56/16). Additional assessments requested (but not required) were CD123+ (dendritic lymphocytes), CD11c+ (dendritic myeloid cells), CD3+CD56+CD16+ (NKT cells), CD45RA+/CD62L+(RTE), CD25+/CD62L+(T-Reg), Total CD25+, CD57+/CD28+(CTL), HLA-DR+(Activated), and quantitative immunoglobulins (and record of intravenous immunoglobulin (IVIg) administrations). In patients enrolled in the optional immune reconstitution sub-study, additional exploratory immunologic parameters were assessed.

9.5.3.16 Health-Related Quality of Life

Patient-reported HRQoL outcomes were assessed during the trial using two standardized measures including the Functional Assessment of Cancer Therapy –Bone Marrow Transplant Module (FACT-BMT) and the EuroQol EQ-5D, which have been reported in previous trials involving BM transplant in patients (McQuellon, Russell et al. 1997, van Agthoven, Vellenga et al. 2001).

9.5.3.17 FACT-BMT

The Functional Assessment of Cancer Therapy –Bone Marrow Transplant (FACT-BMT) Version 4 is a self-administered instrument designed to assess multidimensional aspects of the quality of life (QoL) in BMT patients. It comprised the 27-item FACT-General (FACT-G) that evaluates the HRQoL of patients receiving treatment for cancer and the 23-item Bone Marrow Transplantation Subscale (BMTS) that addresses disease and treatment-related questions specific to BM transplant. The FACT-G assesses four primary dimensions of QoL, including physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), and functional well-being (7 items). A five-point Likert-Type response scale ranging from 0 to 4 is used (0 = ‘not at all’; 1 = ‘a little bit’; 2 = ‘somewhat’; 3 = ‘quite a bit’; and 4 = ‘very much’).

For patients <18 years old, a validated adapted version had been issued, removing nonrelevant items for a pediatric population (seven in total: 2 items from the social/family well-being dimension, two items from functional well-being dimension, and three from the BMTS).

9.5.3.18 EQ-5D

The EQ-5D descriptive system of HRQoL states comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of three responses. The responses record three levels of severity (no problems/some or moderate problems/extreme problems) within a specific EQ-5D dimension.

9.5.3.19 Safety and Tolerability of Omidubicel Transplantation

The safety and tolerability of omidubicel transplantation was evaluated in all patients as described in Section 12. All AEs were coded using MedDRA version 23. Safety related definitions are provided below.

Treatment-Emergent Adverse Event

Treatment-emergent AEs were any AEs that occurred or worsened (i.e., increased in grade) during or after the infusion of either omidubicel or unmanipulated CBU.

Infusion Reactions:
Infusion reactions were conservatively defined as any AE that began or worsened (ie increased in grade) between the start of the graft infusion and 24 hours after the completion of the graft infusion. These events have been described by nature and severity.

Serious Adverse Event

An adverse event or suspected adverse reaction (see Section 9.1.4) was considered "serious" if, in the view of either the investigator or Sponsor, it resulted in one of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect

Important medical events that may not result in death, be life-threatening, or require hospitalization were to be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Causality

The following question was to be used when assessing causality of an adverse event to the study product: Is there a reasonable possibility that the study product caused the event? An affirmative answer designates the event as a suspected adverse reaction.

Anticipated Events Post-Transplant:
These events were collected as described in Protocol Appendix D (Appendix 16.1.1). Events were summarized by severity and time period and described by the MedDRA System Organ Class (SOC), Preferred Term (PT), and relationship to the study product. Maximum toxicity severity for a subject was summarized for each period and for the entire 42-day period.

Unanticipated Events Post-Transplant:
Unanticipated AEs are events not listed in Protocol Appendix D (Appendix 16.1.1) and have been described by the MedDRA SOC, PT, severity, seriousness, and relationship to the study product.

9.5.3.20 Other Definitions

Response Criteria for Acute Leukemia

- Bone Marrow (BM) blasts < 5% by morphologic assessment;
- No circulating leukemic blasts;
- Neutrophil count ≥ 1000/μL;
- Absence of previous cytogenetic or molecular abnormality identified prior to transplantation in the BM aspirate.

Complete Morphologic Remission for CML from Prior Blast Crisis

- BM Myeloblasts < 5% by morphologic assessment;
- No circulating leukemic myeloblasts.

CML Stages

Chronic phase defined as:

- Stable, not hematologic remission: blasts present in marrow and/or peripheral blood, but disease did not qualify as accelerated or blast phase
- Hematological remission: no blast cells or precursor cells in the blood or marrow
- Partial cytogenetic remission: Ph+ metaphases > 0% but < 35%
- Complete cytogenetic remission: absence of Ph+ metaphases

Accelerated phase defined as:

- WBC difficult to control (> 50×10^9/L despite therapy)
- Rapid doubling of WBC (< 5 days)
- Anemia or thrombocytopenia unresponsive to standard treatment
- Persistent thrombocytosis (> 1000×10^9/L)
- Cytogenetic abnormalities in addition to Ph+
- Increasing splenomegaly
- Marrow fibrosis

Blasts Crisis defined as:

- 5% blasts in the marrow not attributed to other causes (e.g., BM regeneration)

Additionally, the response criteria for lymphoma are defined in Table 7.

Table 7: Response Criteria for Lymphoma

Response	Definition	Nodal Masses	Species, Liver	Bone Marrow
CR	Disappearance of all evidence of disease	a. FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative b. Variably FDG-avid or PET negative; regression to normal size on CT	Not palpable, nodules disappeared	Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunohistochemistry should be negative
PR	Regression of measurable disease and no new sites	≥ 50% decrease in SPD of up to six largest dominant masses; no increase in size of other nodes a. FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site b. Variably FDG-avid or PET negative; regression on CT	≥ 50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen	Irrelevant if positive prior to therapy; cell Type should be specified
SD	Failure to attain CR/PR or PD	a. FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET b. Variably FDG-avid or PET negative; no change in size of previous lesions on CT		
Relapse disease or PD	Any new lesion increase by ≥50% or previously involved sites from nadir	Appearance of a new lesion(s) > 1.5 cm in any axis, ≥ 50% increase in SPD of more than one node or ≥50% increase in longest diameter of a previously identified node >1 cm in short axis Lesions PET positive if FDG-avid lymphoma or PET positive prior to therapy	≥ 50% increase from nadir in the SPD of any previous lesions	New or recurrent involvement

Data Source: Protocol GC P#05.01.020 (Appendix 16.1.1)

Abbreviations: CR: Complete remission; FDG: [^{18}F] fluorodeoxyglucose; PET: Positron emission tomography; CT: Computed tomography; PR: Partial remission; SPD: Sum of the product of the diameters; SD: Stable disease; PD: Progressive disease.

9.5.4 Physical Examination

Physical examinations were conducted during screening, conditioning, and on Days 0, 28, 70, 100, 180, 270, and 365 post-transplantation. Additionally, physical examinations included standard of care cardiac and pulmonary monitoring.

9.5.5 Clinical Laboratory Evaluation

Clinical laboratory evaluations were conducted according to Table 8, and all laboratory measurements were evaluated for abnormalities. Study physicians were responsible for interpreting abnormal laboratory values in context of the disease and condition leading to it. Reported abnormal laboratory values that were considered AEs were graded using the CTCAE Toxicity Grading Scale Version 4.03.

9.5.6 Schedule of Events

Table 8 presents the schedule of events for all study visits.

Table 8: Schedule of Events

	Schedule of Assessments Summary																	
	Baseline			Transplantation and Follow-Up														
	Screening	Prep		Days Post-transplant														
	Within three weeks prior to randomization	From randomization to conditioning [1]	Conditioning	0	1	2-6	7[18]	14 ±3	21 ±3	28 ±3	35 ±3	42 ±3	56 ±3	70 ±3	100 ±14	180 ±21	270 ±21	365 ±21
Identify qualifying CBUs [2]	X																	
Written Informed Consent[3]	X																	
Eligibility Criteria[4]	X																	
Confirm transplant suitability within 24 hours prior to conditioning		X																
Omidubicel arm: CBU sent to the production site to arrive no later than two working days before the start of manufacturing		X																
Medical History	X																	
Infectious disease markers [5]	X																	
Anti-HLA antibodies[6]	X																	
Cardiac: EKG, Echocardiography or MUGA scan with LVEF [7]	X																	
Chest X-ray [7]	X																	
Pulmonary Function Tests (prior to treatment with bronchodilators) with cDLCO, FEV1, FVC, and oxygen saturation[7]	X																	
Serum or urine beta HCG (females)[29]	X[24]																	
Confirmatory HLA typing[8]	X																	
BASELINE DISEASE ASSESSEMENT[9] All patients: when clinically indicated, PB and BM morphology (aspiration, and biopsy if applicable) Leukemia/MDS: BM FACS analysis (flow cytometry), cytogenetics, and molecular markers Lymphoma: CT scan or PET-CT chest, abdomen, pelvis	X																	

		Schedule of Assessments Summary																	
		Baseline			Transplantation and Follow-Up														
		Screening	Prep		Days Post-transplant														
		Within three weeks prior to randomization	From randomization to conditioning [1]	Conditioning	0	1	2-6	7[18]	14 ±3	21 ±3	28 ±3	35 ±3	42 ±3	56 ±3	70 ±3	100 ±14	180 ±21	270 ±21	365 ±21
Disease assessment follow-up																			
Leukemia MDS	Clinical evaluation for relapse per physician's judgment										X					X	X		X
	BM morphology															X			X
	CBC with differential										X						X		
	FACS analysis (flow cytometry)[26]															X	X		X
	Cytogenetics and molecular markers[27]															X			X
	Further tests as clinically indicated										X					X	X		X
CML	Clinical evaluation for relapse per physician's judgment										X				X	X	X		X
	Quantitative RT-PCR BCR/ABL in peripheral blood[28]														X	X	X		X
	Further tests as clinically indicated										X				X	X	X		X
Lymphoma	Clinical evaluation for relapse per physician's judgment										X					X	X		X
	BM morphology as clinically indicated																		X
	CT- Scan or PET-CT															X			X
	Further tests as clinically indicated										X					X	X		X
Vital Signs[10]		X[11]		X	×10	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory (CBC and Chemistry) [12]		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Historical and Concomitant medications[13]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Karnofsky/Lansky performance score		X																	X
Physical Examination		X		X	X						X[14]				X[14]	X[14]	X[14]	X[14]	X[14]
Complete urinalysis with microscopic analysis		X																	
Immunophenotyping Lymphocyte subsets[15]											X				X	X	X		X
Peripheral blood sample for Chimerism[16]		X																	
Peripheral blood chimerism[17]										X			X			X	X		X
Conditioning regimen as per protocol				X															

	Schedule of Assessments Summary																	
	Baseline			Transplantation and Follow-Up														
	Screening	Prep		Days Post-transplant														
	Within three weeks prior to randomization	**From randomization to conditioning [1]**	**Conditioning**	**0**	**1**	**2-6**	**7[18]**	**14 ±3**	**21 ±3**	**28 ±3**	**35 ±3**	**42 ±3**	**56 ±3**	**70 ±3**	**100 ±14**	**180 ±21**	**270 ±21**	**365 ±21**
Omidubicel arm: Omidubicel CF, NF, and infusion solutions shipped to clinical site before or during conditioning Control Arm: CBU sent to the clinical site before or during conditioning		X	X															
Stem cell (omidubicel CF/NF, UCBU(s), or other) thawing and infusion				X														
Toxicity assessment 24 hours post infusion				X	X													
Assess Acute GvHD							X	X	X	X	X	X	X	X	X	X		
Assess Chronic GvHD															X	X	X	X
CMV PCR			X[19]				X	X	X	X	X	X	X	X	X			
EBV PCR									X				X		X	X[20]	X[20]	X[20]
HHV6 PCR until ANC > 500							X	X	X	X	X	X						
HRQoL patient self-report questionnaires[25]	X											X			X	X		X
Optional supplemental immune reconstitution sub-analysis – blood sample collection [23]	X						X	X	X	X		X	X	X	X	X		X
Between Visit Monthly Check Up[21]															X[21]			
15-month post-randomization survival and relapse status[22]																	X	
Infections		Infections collected from randomization until end of study																
AEs	From time of consent until end of study																	
Hospital Admission			From start of conditioning regimen until end of study															

Source: Protocol GC P#05.01.020 (Appendix 16.1.1)

[1] The time between randomization and conditioning varies by treatment and may be further delayed due to changes in the patient's health. In the event of a failure to transplant the patient by Day 90 post-randomization, an assessment of survival, relapse history, infection history, and HRQoL (optional, if possible) are required at days 90, 130, 210, and 365 post-randomization (or more frequently as clinically indicated) as well as an assessment of survival and relapse history at 15 Months post-randomization.

[2] Before signing informed consent and according to CBUs matching criteria as detailed in the protocol. After consent, the CBU documents for the CBU selected for expansion (treatment CBU #1) must be redacted and uploaded to Advantage eClinical ® prior to randomization.

[3] Signed consent is required prior to performing any protocol specific tests or procedures that are not part of the standard site practice. The ICF signature can be obtained earlier than 3 weeks prior to randomization.

[4] All eligibility criteria must be met prior to randomization. Unless otherwise indicated, screening and eligibility testing must be performed and resulted within three weeks prior to randomization.

[5] Infectious disease markers must include: HIV I/II Ab, HTLV I/II Ab, HBsAg, HBcAb, HCV Ab, VZV Ab, syphilis Ab (such as RPR), EBV Ab, and CMV screen (IgG or Total).

[6] Tests performed within 4 weeks prior to randomization are acceptable.

[7] Test results from within 9 weeks prior to randomization are acceptable. Chest X-ray is not mandatory if a chest CT or MRI was performed.

[8] Verification typing (confirmatory typing) must be performed and resulted prior to CBU shipment to the production site. Extended high-resolution typing at HLA -A, -B, -C, -DRB1 is also required for the patient and CBU#1 but (with the exception of -DRB1) can be performed after randomization unless anti-HLA antibody testing reveals a positive result (MFI>3000) at HLA-A, B, C, or DRB1. If assigned to the control arm and treatment CBU #2 is selected, then HLA -A, -B, -C, -DRB1 high-resolution typing is also required for treatment CBU #2; ABO and Rh typing is also required for the patient, CBU#1 and CBU#2 (if applicable).

[9] Baseline disease assessment should be as close as possible to randomization to minimize findings of relapse during CBU expansion. Specific requirements for the timing of this assessment are provided in Section 9.4.5 T scan (for lymphoma patients); tests from within 9 weeks prior to randomization are acceptable. For MDS and CML patients, biopsy should have been performed within one year prior to transplant and should be repeated prior to transplant if fibrosis was noted on a prior biopsy. For ALL, AML, and other leukemia (not including MDS and CML) patients an aspiration is sufficient. FACS analysis/flow cytometry is required prior to randomization for AML, ALL and other leukemia (not including MDS and CML) patients and required prior to conditioning for CML and MDS patients. For Leukemia/MDS patients, cytogenetics and molecular markers may be done after randomization prior to conditioning (it is not mandatory to repeat molecular markers tests that were negative at diagnosis).

[10] Temperature, blood pressure and pulse at all visits; Weight through Day 100 visit Respiratory rate through Day 1 post-transplant.

[11] Including height, weight, and BSA.

[12] CBC performed at screening, daily from Day 0 until neutrophil engraftment, and at all study visits post-transplant. Differentials required if WBC ≥ 0.5. Blood chemistries must include (at a minimum): serum creatinine, total bilirubin, alkaline phosphatase, AST, ALT, and magnesium (at screening, Day -1 (creatinine only), Day 0 and then at least twice weekly until Day 28, and weekly after Day 28 until 10 weeks post-transplant; at 100 days, 6 months, 9 months, and 1 year post-transplant).

[13] All concomitant medications and blood products administered, including total number of RBC and platelet units transfused, from time of signature on the IC until the end of the study, will be recorded in the source documents and the reason for administration should be clearly stated. Concomitant medications will also be recorded in the eCRF as detailed in the Data Management Handbook.

[14] Including standard of care cardiac and pulmonary monitoring.

[15] On Days 28, 70, 100, 180, and 365, site will perform a basic lymphocyte subset analysis (CD3, CD4, CD8, CD19, CD56/16) locally. Additional assessments requested (but not required) are: CD123+ (dendritic lymphocytes), CD11c+ (dendritic myeloid cells), CD3+CD56+CD16+ (NKT cells), CD45RA+/CD62L+(RTE), CD25+/CD62L+(T-Reg), Total CD25+, CD57+/CD28+(CTL), HLA-DR+(Activated), and quantitative immunoglobulins (In case quantitative immunoglobulins are assessed, a record of the most recent IVIG administrations is required).

[16] Patient sample will be obtained anytime during the screening period or post-randomization prior to the initiation of the conditioning regimen; CBU sample will be shipped to the clinical site along with the UCBU or omidubicel product.

[17] Measured by molecular methods, in whole blood at Day 21 or Day 28 and at Days 42, 100, 180, and 365. BM chimerism is an acceptable alternative.

[18] Day 7 GvHD assessment must be done on Day 7 post-transplant. All the other Day 7 assessments can be done until Day 10 post-transplant included.

[19] All recipients must be tested for CMV (using the PCR method) at least once during the conditioning period.

[20] Not required if patient no longer on immunosuppression.

[21] Beginning after the Day 100 visit, the site will continue at least monthly contact with the subject until Day 365 visit. If there is no hospital or clinic visit scheduled at the transplant center for more than 30 days, then a member of the study team will contact the subject via phone or email within 35 days from the last contact to inquire about AEs, hospitalizations, infections, and medication changes (including transfusions). This contact will be documented in the subject's medical or research record.

[22] The patient survival and relapse status should be assessed at 15 Months or later post-randomization.

[23] Samples to be shipped to a central laboratory for analysis.

[24] Serum or urine beta HCG can be collected up to 4 weeks before randomization.

[25] HRQoL not required if a survey is not available in the patient's primary language. Refer to Protocol Section for details on HRQoL administration (Appendix 16.1.1).

[26] Flow cytometry on BM or PB sample if judged necessary by the treating physician.

[27] It is not mandatory to repeat molecular markers tests that were negative at diagnosis.

[28] If positive: BM aspirate with morphology, cytogenetics, and quantitative RT-PCR BCR/ABL.

[29] Serum or urine beta HCG can be collected up to 2 weeks before randomization.

Abbreviations: Ab: Antibody; AE: Adverse event; ALL: Acute lymphoblastic leukemia; ALT: Alanine aminotransferase; AML: Acute myelogenous leukemia ; ANC: Absolute neutrophil count; AST: Aspartate aminotransferase; BCR: Breakpoint cluster region gene; BM: Bone marrow; BSA: Body surface area; CBC: Complete blood count CBU: Cord blood unit; cDLCO: Diffusing capacity of the lungs for carbon monoxide; CF: Cultured fraction; CMV: Cytomegalovirus; CT: Computed tomography; EBV: Epstein-Barr virus; eCRF: Electronic case report form; EKG: electrocardiogram; FEV1: Forced expiratory volume; FVC: Forced volume capacity; GvHD: Graft-versus-host disease; HBcAb: Hepatitis B core antibody; HBsAg: Hepatitis B surface antigen; HCG: Human chorionic gonadotropin; HCV Ab: Hepatitis C antibody; HHV6: Human herpesvirus 6; HLA-DR: Human leukocyte antigen – DR isotype; HRQoL: Health-related quality of life; HTLV I/II Ab: Human T-lymphotropic virus I/II antibody; IC: Informed consent; MRI: Magnetic resonance imaging; MUGA: Multigated acquisition scan; MDS: Myelodysplastic syndromes; NF: Non-cultured fraction; PB: Peripheral blood; PCR: Polymerase chain reaction; RBC: Red blood cell; RPR: Rapid plasma reagin; RT-PCR: Reverse transcription polymerase chain reaction; UCBU: Unmanipulated cord blood unit; VZV Ab: Varicella zoster virus antibody; WBC: White blood cell.

9.5.7 Appropriateness of Measurements

9.5.7.1 Primary Endpoint

As the purpose of this study was to compare the safety and efficacy of omidubicel transplantation to unmanipulated CBU transplantation in patients with hematological malignancies, the time to neutrophil engraftment following transplantation was selected as the primary endpoint, which has been identified as a clinically meaningful endpoint as supported by publicly available clinical literature and FDA and EMA Agency correspondence regarding the study design (FDA Meeting Response 2017, EMA Scientific Advice Letter 2015). Specifically, neutrophil engraftment was defined as achieving an ANC $\geq 0.5 \times 10^9$/L on three consecutive measurements on different days with subsequent donor chimerism ($\leq$ 10% host cells by peripheral blood chimerism, or by BM chimerism if peripheral blood chimerism is not available) any time on or after the day of engraftment up to the earlier of Day 100 post-transplant, date of relapse, date of secondary graft failure, or date of death. The first day of the three ANC measurements was designated the day of neutrophil engraftment and had to occur on or before 42 days post-transplant and prior to any competing risks.

The primary endpoint was selected because early engraftment following umbilical CBT represents a clinically meaningful outcome and offers an objective, easily measured endpoint in this orphan patient population. To extrapolate, prompt and robust engraftment of neutrophils is considered the most notable milestone in hematopoietic recovery following stem cell transplantation and has been identified as an early indication of treatment success as demonstrated by the clinical consequences associated with the delay in neutrophil engraftment observed in CBT compared to other stem cell sources (Brunstein, Gutman et al. 2010, Eapen, Rocha et al. 2010). Importantly, it has been identified that delayed engraftment is the single greatest barrier to successful CBT and is the most important contributor to early non-relapse mortality (NRM) (Brunstein, Gutman et al. 2010). Delayed hematopoietic recovery can result in an increased occurrence or higher severity of complications after transplantation. This may lead to substantial organ damage, which may be irreversible, and death. The substantial reduction of the time to engraftment reported in the primary analysis is thus clinically meaningful, decreasing the duration of life-threatening neutropenia following myeloablative conditioning by half.

Moreover, publicly available clinical literature from international studies reports similar hematopoietic recoveries for both double and single CBT, with median 22 and 23 days to neutrophil engraftment in adults (Ruggeri, Labopin et al. 2014, Barker, Fei et al. 2015). In addition, studies investigating differences in outcomes between umbilical CB and other graft sources consistently report higher mortality following CBT, generally attributable to inadequate hematopoietic recovery (Brunstein, Gutman et al. 2010, Eapen, Rocha et al. 2010).

9.5.7.2 Secondary Endpoints

The secondary endpoints included incidence of Grade 2/3 bacterial or invasive fungal infections by 100 Days post-transplantation, days alive and out of hospital in the first 100 Days post-transplantation, and platelet engraftment by 42 days post-transplantation. The

secondary endpoints were selected to further investigate the clinical benefit and to further characterize the overall risk-benefit profile of omidubicel.

Events of infections and prolonged hospitalization, as well as NRM, reflect the clinical sequelae of delayed hematopoietic recovery, further supporting the clinical meaningfulness of the primary endpoint. Rapid hematopoietic recovery is thus anticipated to reduce the risk of infections. In particular, bacterial and fungal infections predominate in the early months following transplant and are dependent on rapid and robust neutrophil recovery (Hamza, Lisgaris et al. 2004, Yazaki, Atsuta et al. 2009). Therefore, a secondary endpoint is the incidence of bacterial infections (Grade 2-3) and invasive fungal infections occurring up to 100 Days post-transplant.

Prolonged hospitalization is an additional clinical sequela of delayed hematopoietic recovery in CBT recipients as demonstrated in a 100-day study comparing duration of hospitalization among 1577 patients with acute leukemia in remission receiving umbilical CB, match unrelated donor (MUD) or mismatched unrelated donor (MMUD) HSCT (Ballen, Joffe et al. 2014). Multivariate analysis results demonstrated that umbilical CB recipients had fewer days alive and out of hospital compared to other graft sources (Ballen, Joffe et al. 2014). Therefore, assessing the number of days each subject is alive and out of hospital in the first 100 Days post-transplantation has been selected as a secondary endpoint.

In the process of successful recovery following HSCT, neutrophil engraftment is gradually followed by the recovery of additional hematopoietic cell lineages. Delayed platelet engraftment is a frequent complication after CBT and is associated with increased non-relapse mortality (NRM) and poorer overall survival. Specifically, it has been demonstrated that platelet counts predict the risk of chronic GvHD development and mortality following allogeneic PB transplantation and that delayed platelet recovery is most common following CBT (Kim, Sohn et al. 2006, Ramírez, Brunstein et al. 2011). Therefore, the time from transplantation to platelet engraftment was assessed and platelet engraftment by 42 days was selected as a secondary endpoint.

9.5.7.3 Tertiary and Exploratory Endpoints

Post-transplant complications may result in death, and thus transplant-related mortality, as reflected by NRM at 210 days following randomization (approximately six months post-transplant) was assessed as a tertiary endpoint.

Viral infections occur throughout the first year post-transplant, in parallel to the recovery of the immune system. Therefore, Grade 3 viral infections were assessed at 180 days and 1 year following transplantation. These events were assessed in the context of the exploratory endpoints as a safety assessment, where omidubicel was anticipated to be no worse than controls.

Omidubicel *ex vivo* expansion is aimed to provide rapid hematopoietic recovery, overcoming the known delay in CBT compared to other graft sources. Thus, neutrophil engraftment by 16 Days following transplantation was assessed as an additional exploratory endpoint, a cutoff which reflects the usual time of neutrophil engraftment in matched peripheral blood donor transplants (Storek, Dawson et al. 2001, Eapen, Rocha et al. 2010).

9.6 Data Quality Assurance

This study was conducted in compliance with the requirements of the Declaration of Helsinki and ICH/GCP guidelines along with the sponsor's and CRO's SOPs, protocols and best practices.

Data quality checks were performed through a variety of methods. Within the electronic data capture (EDC) system, Advantage eClinical, automated reports were produced to identify missing forms, missing values, and monitoring discrepancy reports. A manual query report also provided a listing of all queries identified by Emmes or the site Clinical Research Associate (CRA) for site resolution.

Source data verification was performed by CRAs, and data verification results were reported in the Protocol Monitoring module of Advantage eClinical. Monitoring was performed as outlined in the Site Monitoring Plan as described in the study protocol (Appendix 16.1.1) according to a risk-based approach where select forms were fully monitored, and others monitored at a reduced rate as agreed upon by Emmes and the Sponsor. Monitoring took place both on site and remotely based on the capabilities of each site. Central Monitoring reports were distributed by the Emmes Lead CRA approximately monthly to the local site CRA. These reports reviewed specific CRFs to provide support to the local CRA and to ensure consistency in monitoring across all study sites. CRAs also performed remote monitoring of CRFs on an ongoing basis for those forms where the site staff uploaded redacted source documents as requested per the Data Management Handbook. These were reviewed through the file attachment feature of Advantage eClinical to aide in more real time review of certain data so that on-site activities could be utilized for other source data review purposes.

9.6.1 Site Training

Training on the protocol and study-specific procedures and reporting, including omidubicel product logistics, was provided to investigators and study site staff at investigator meetings, site initiation visits, and continuously as new staff joined the study according to his/her role. Ongoing training for study staff was provided through monthly team calls to update on a wide range of study activities including but not limited to protocol modifications, database updates, and specific study workflow topics to aide with better understanding and study compliance. Targeted retraining was provided by site CRAs following identification of recurrent or important deviations at the site.

Additional training for database access was required by staff designated that role. CRO staff were trained by Emmes, and it was the responsibility of the site CRA to provide database and data quality training to the study staff. Designated study personnel were trained to use the Advantage eClinical during in-person or web-based training sessions. Following these sessions, study personnel were required to complete a data management practicum. Study personnel were provided access to the EDC system once they had demonstrated sufficient knowledge of data entry in the system.

9.6.2 Site Qualification

A Pre-Study visit (PSV) was required for each selected site and performed according to the applicable CRO SOPs. However, sites that had previously participated in one of the sponsor's clinical interventional studies could have been exempt from a PSV pending sponsor approval. Additionally, a site could have been exempt from the PSV via signed waiver.

A Site Initiation Visit was required for each site and performed according to Experior SOPs. Essential required regulatory documents listed on the Site Activation Form were obtained by the CRA or designee for filing in the Trial Master File (TMF) prior to site activation including IRB approval of the protocol and receipt of approved ICF.

At the time of site activation and with collection of required training (as applicable) site staff were granted access to Advantage eClinical and the study website where all study-related documents and forms were posted.

9.6.3 Site Monitoring

All site monitoring activities were conducted in accordance with ICH GCP E6, 21 CFR 312.50 as described in the Monitoring Plan (Appendix 16.1.1). The monitoring designees- The Emmes Company, LLC and Experior, S.L.- performed monitoring activities in accordance with Experior's SOPs and guidelines as well as sponsor-approved deviations from these SOPs/guidelines to allow for variation between US and EU methodology. Additional CROs and/or freelance CRAs operating under either Experior or the sponsor's project management were required to perform monitoring activities in accordance with Experior's SOPs.

On-site and remote monitoring of electronic case report forms (eCRFs) were utilized as described in the Monitoring Plan (Appendix 16.1.1) to ensure adherence to ICH GCP guidelines and the protocol. Remote monitoring was allowed for this study, and further utilized in support of sites' efforts to keep patients and staff safe from potential exposure to COVID-19, as discussed in Section 9.8.2.

9.6.4 Data Generation and Analysis

Custom eCRFs were designed for this study to capture data generated. The EDC system was developed and maintained by Emmes' Data Coordinating Center (DCC). The EDC system used to conduct this study was developed by The Emmes Company and is 21CFR part 11 compliant. Additionally, a data quality review was conducted monthly as described in the Data Management Plan. A sample eCRF is provided in Appendix 16.1.2. Authorized users were queried on data inconsistencies and made corrections to the data as needed as described above. All modifications to eCRFs were tracked via audit history in Advantage eClinical, prior to a database freeze.

9.7 Planned Statistical Methods and Determination of Sample Size

9.7.1 Statistical and Analytical Plans

9.7.1.1 Study Design and Objectives

The study is designed as an open-label, controlled, multicenter, Phase III, randomized study of transplantation of omidubicel versus unmanipulated CBU in patients with hematologic malignancies.

9.7.1.2 Accrual

The study enrolled 125 patients, randomized in a 1:1 ratio to the omidubicel, and control arms. The study accrual was designed so that no single site accounted for an unusually large fraction of patients.

Formal sample size calculation for the primary endpoint showed that 72 patients were needed to provide 90% statistical power (see section 9.7.2). Nevertheless, the study included a larger number of patients so as to provide a larger safety database for omidubicel, a better understanding of its comparative effects on other endpoints, and very high power to detect an effect on the primary endpoint.

9.7.1.3 Randomization

The study utilized minimization, which is a form of randomization designed to ensure that treatment groups are well-balanced with respect to selected factors of prognostic importance. There were four factors included in the minimization algorithm: treatment center, disease risk group, age group, and intent to perform single vs. double cord transplant in the control arm.

A total of 33 treatment centers were included. The disease risk group definition, which is based on the "refined DRI" had three levels: low risk, moderate risk, and high/very high-risk (Armand, Kim et al. 2014). The risk group was assigned by applying the criteria of Armand et al. for DRI assignment and was further adjusted to include in high/very high-risk group any AML, ALL and other leukemia (not including MDS and CML) patient with any level of MRD detected by flow cytometry(Armand, Kim et al. 2014). For patients with rare disease types who are not classified by Armand et al, the disease risk was assigned by the site investigator. The age group factor had three levels: 12-17 years, 18-39 years and $\geq$ 40 years. Although age and disease/stage may not strongly influence the primary endpoint, there was an advantage in keeping them well-balanced across the treatment groups for the purposes of comparing other important endpoints, including overall mortality and NRM. Although all the patients treated with omidubicel received a transplant from a single CBU source, the intent to perform single vs. double cord transplant was included as a factor in the randomization algorithm to address potential imbalances resulting from differences in CBU selection based on the patient weight or HLA matching options.

To implement the minimization randomization, a measure of treatment group imbalance was calculated for each new patient. For a given patient, the algorithm compared the numbers of patients previously assigned to omidubicel at the same levels of the four factors as the current patient to the numbers of patients on umbilical CB at the same levels of the four factors as the current patient. Depending on the number of matches in each treatment group, the DRI assigned patients to a stratum and chose the next treatment assignment in that strata. A

random element was included in the assignment, whereby when the minimization algorithm indicated a preference to allocate a specific treatment, say omidubicel, then that treatment was allocated with probability 0.9. Whenever the imbalance measures were equal under the two allocations, a probability of 0.5 was used.

9.7.2 Determination of Sample Size

The primary endpoint was time from transplant to neutrophil engraftment. The primary analysis for comparing time to engraftment between the two treatment groups was based on the Mann-Whitney test statistic (Appendix 16.1.9). This test was shown to be equivalent to using a Gehan-Wilcoxon alternative in a time-to-event analysis with competing risks. Although the test was based on the re-randomization distribution, rather than the usual permutation distribution or its normal approximation, little or no statistical power was lost thereby, as confirmed by simulations. The primary sample size calculations were therefore based on the usual methods associated with the Mann-Whitney test. Noether's formula was used to calculate the sample size.

Noether's formula requires specifying the probability P that an omidubicel patient has a shorter engraftment time than a control patient. The estimate of this probability was based on data from 16 patients treated with a single cord omidubicel transplant and 152 patients in the CIBMTR registry database treated with CBT from 2010-2013 and with criteria that would make them eligible for the omidubicel study, including the criteria for the CBUs.

Based on these datasets and factoring in adjustments, assuming (a) that 10% of patients allocated omidubicel would fail to receive a transplant compared to 4% of patients allocated unmanipulated CBU and (b) that 5% of patients allocated omidubicel would receive not omidubicel but unmanipulated CBU due to failure of the omidubicel expansion, the estimate of P was 0.78. A pessimistic estimate that is one standard error lower than the estimate of 0.78 was 0.72.

Noether's formula for a trial using a two-sided significance level of 5% and having 90% statistical power gave a total sample size of 45 for P=0.78 and 72 for P=0.72.

Although the formal sample size calculation for the primary endpoint provided above yielded a size between 45 and 72, the study was designed to be larger for the following reasons:

- to provide a more extensive safety database for omidubicel;
- to ensure that statistical significance on the primary endpoint would be very strong and highly convincing; and
- to reduce the chance of seeing higher mortality in the omidubicel group than in the control group even if omidubicel truly has a beneficial effect on mortality.

For these reasons and in consideration of the orphan indications, a total sample size of 120 patients was planned, with approximately 60 randomized to omidubicel and 60 to control. With 120 patients, statistical power for the primary endpoint was estimated to be > 0.99.

9.8 Changes in the Conduct of the Study or Planned Analyses

9.8.1 Changes in the Conduct of the Study

A summary of protocol amendments is presented in Appendix 16.1.1. A total of seven version amendments were included in addition to four local amendments. The initial study protocol was dated March 08, 2016. Many of the amendment changes were implemented based on investigator and site feedback to align the protocol more with standard criteria and/or assessment schedules at clinical sites. Country-specific versions were issued as required by the country to meet specific regulations and were incorporated as applicable in subsequent amendments.

Table 9: Summary of Protocol Amendments

Amendment	Date / Number of Randomized Patients Prior to Amendment (%)	Major Changes
Amendment I	August 05, 2016 / 0	• Addition of NRM at 210 Days post-randomization as a secondary endpoint; Addition of NRM assessment at 1-year following randomization; Addition of Day 28 timepoint for immune reconstitution. • Updated disease inclusion criteria for AML and ALL, TBI dose and days for conditioning regimen option A.2. • Determination of using a single or double cord in the control arm by the investigator prior to randomization was clarified and general language clarifications/refinements were made.
Amendment II	October 27, 2016 / 0	• Updated secondary endpoint assessment dates for NRM, OS and DFS, relapse, and relapse mortality from one year to 15 Months post-randomization. • AE collection time changed from initiation of conditioning regimen to time of consent. • Added clarification of omidubicel infusion guidelines, including minimal infusion time. • BM assessment changed from Day 270 to Day 365 post-transplant. • Updates made to GvHD prophylaxis monitoring levels and the final process quality control testing and release criteria.
Amendment III	July 30, 2017 / 7 (5.6%)	• MDS disease criterion and MDS baseline disease assessment criterion were updated. • Adjustments were made to refine logistic processes of CBU review to simplify study enrollment and workflow.
Amendment IV	December 10, 2017 / 13 (10.4%)	• Expanded eligibility criteria to include ALL, AML, and MDS patients and to patients with lymphoma and other rare hematologic malignancies that are typical candidates for transplant. • Patient age adjusted from 16-60 years to 12-65 years to allow for a wider age range. • Lansky performance scale added due to the inclusion of pediatric patients. • Further clarification to the CBU logistic and review processes were made, as well as simplification of backup CBU criteria. • Endpoint label modifications made per FDA request to separate into secondary, tertiary, and exploratory endpoints. • NRM was changed from a secondary to tertiary endpoint. • Details of when chimerism testing must show donor cells to be considered neutrophil engraftment were added. • Updates to GvHD and infection prophylaxis and recommendations for toxoplasmosis prophylaxis were added. • Language for post- transplant assessments was updated to clarify required days of assessments and distinguish between required versus requested or as performed per standard of care assessments.

Amendment	Date / Number of Randomized Patients Prior to Amendment (%)	Major Changes
		• Patient survival and relapse status assessment at 15 Months or later post-randomization was added. • Release criterion for the omidubicel CF was updated to include viability of CD34+ cells.
Amendment V	May 01, 2018 / 27 (21.6%)	• Additional (optional) sub-studies for long-term follow-up and immune reconstitution testing were added. • Eligibility criteria for ALL, CML, MDS, and lymphoma broadened to align more with standard criteria for transplant candidates, together with disease baseline assessments. • Site selection of conditioning regimen of choice broadened so clinical sites could select a regimen according to primary diagnosis/age group instead of relying solely on one regimen for all patients. • Permission for GvHD prophylaxis adjustments depending on patient diagnosis or age group. • Regimen A.2 modified to allow for TBI to be given as either 1320 cGy or 1200 cy total per institutional practice. • Calculation for adjusted body weight formula modified to be specific for the regimen selected. • Calcineurin inhibitor tapering was adjusted to allow to begin at Day 100 instead of Day 150. • Amendment V was recalled by Gamida Cell from submission to sites as of May 14, 2018, and CROs notified accordingly, following a meeting with FDA that required implementation of changes to the protocol.
Amendment V.1	May 22, 2018 / 29 (23.2%)	• Provided to sites for submission included all changes made in Amd V • Updates added regarding required disease assessment including flow cytometry, cytogenetics, molecular markers and/or BM morphology and other applicable assessments for all randomized patients at specified visits prior to visit on Day 365 post-transplant per FDA request.
Amendment VI	January 22, 2019 / 55 (44.0%)	• Addition of new disease criterion of CMMoL and MDS/CMMoL overlap to broaden the list of rare diseases allowed per study. • Wording adjustments to ALL and MDS criteria. • Screening test results requirements adapted to accommodate a pediatric population. • Regimen A.1 modified to allow for TBI to be given as either 1350 cGy or 1200 cy total as per institutional practice. • Regimen B modified to allow for an alternate dose of busulfan to be added. • FACT-BMT quality of life assessment modified for pediatric population. • Lymphoma disease assessment was updated to allow for either CT or PET-CT scan of chest, abdomen, and pelvis at baseline and post-randomization. • Chimerism assessment allowed to be performed as whole blood or myeloid fraction at the required study visit days.

Amendment	Date / Number of Randomized Patients Prior to Amendment (%)	Major Changes
		• Release criteria tables for the CF, NF, and infusion solution were removed from the protocol as the Certificates of Analysis are provided to the site by Gamida Cell for each batch product to inform of all product specifications. • Clarification of SUSAR reporting for omidubicel arm only and based on Regulatory Authorities requirements. • All modifications in local amendments IV.1 and IV.2 were included in this Amendment VI.
Country-Specific (Local) Amendments		
Amendment IV.1	August 28, 2018 / 39 (31.2%)	UK local amendment following request from MHRA (UK competent authority). • Integration of criteria for inclusion of MDS patients considered high-risk per IPSS-R (Revised); this MDS criterion had been an approved protocol waiver and was incorporated into the main Amendment V /V.1. • Language regarding acceptable methods of contraception was clarified, as well as a change in pregnancy test window from 4 weeks to 2 weeks prior to randomization. • Clarification on safety reporting and site/sponsor responsibilities were added. • These changes were incorporated into the subsequent Amendment VI.
Amendment IV.2	October 16, 2018 / 43 (34.4%)	UK local amendment following additional request from REC (UK Central EC). • Wording added to ensure timelines from randomization to transplant will be discussed with the patient, underlying the 3-week difference between control and omidubicel arm. This change was incorporated into the subsequent Amendment VI.
Amendment VI.1	May 29, 2019 / 70 (56.0%)	France local amendment following the « Agence nationale de sécurité du médicament et des produits de santé » (ANSM) (France Medical Authority) request to enable local recommendations. • Disease eligibility criteria wording was clarified to allow the use of more stringent local guidelines if applicable; updates also applied to exclusion criteria for patients with an 8/8 allele level HLA-matched readily available donor. A statement was added in conditioning regimen section to remind investigators to reference the available summary of product characteristics in France for patient management and contraindications. Recommendation for a pregnancy test, when applicable, was added to the assessments requested prior to conditioning.
Amendment VI.2	May 30, 2019 / 70 (56.0%)	UK local amendment following a request from the clinical site Royal Marsden Hospital, London • Update to accommodate local pharmacy standard practice and allow chemotherapy dose banding for conditioning regimens where is it the institutional standard, and upon agreement with the sponsor.

Data Source: Appendix 16.1.1
Abbreviations: AE: Adverse event; ALL: Acute lymphoblastic leukemia; AML: Acute myelogenous leukemia; BM: Bone marrow; CBU: Cord blood unit; CF: Cultured fraction; CML: Chronic myelogenous leukemia; CMMoL: Chronic myelomonocytic leukemia; CROs: Contract research organizations; CT: Computerized tomography; DFS: Disease-free survival; FACT-BMT: Functional Assessment of Cancer Therapy – Bone Marrow Transplant Module; GvHD:

Graft-versus-host disease; HLA: Human leukocyte antigens; IPSS-R: Revised International Prognostic Scoring System; MDS: Myelodysplastic syndrome; MHRA: Medicines and Healthcare Products Regulatory Agency; NF: Non-cultured fraction; NRM: Non relapse mortality; OS: Overall survival; PET-CT: Positron emission tomography-computerized tomography; REC: Research Ethics Committee; SOC: Standard of care; SUSAR: Suspected unexpected adverse reactions; TBI: Total body irradiation.

9.8.2 Changes Related to the COVID-19 Pandemic

In response to the emergence of the COVID-19 pandemic during the study follow-up period, several actions were taken to mitigate any potential risks to study patients and potential negative impacts on data integrity. Sites were provided with a detailed survey to assess any practice changes that may have impacted patient follow-up or care for all study patients under the period of COVID-19. Twenty-seven sites responded to the survey, representing 55 of 57 patients potentially affected by the COVID-19 public health emergency. Site responses did not indicate any changes that would have impacted the endpoints of the study. Changes to standard practice included:

- addition of COVID-19 specific testing requirements and patient education
- use of telemedicine, home visits and local labs to limit potential exposure
- visitor limitations and masking requirements
- one site indicated some delays in getting lab results
- completion of HRQoL Questionnaires at home

There was no indication of any changes in:

- the likelihood or length of hospitalization
- frequency of non-COVID infection surveillance
- threshold to initiate infection workup and testing for respiratory symptoms
- antimicrobial prophylaxis or treatment
- platelet transfusion policies
- frequency or timing of disease assessments
- frequency of lab testing

A listing of survey results including all changes in practice indicated by the sites is included in Listing 16.2.2.12.

Survey results established March 2020 as the time when most sites implemented COVID-19-related practice changes; therefore, March 15, 2020 was selected as a pivot-point for follow-up conducted before or during COVID-19 practice changes.

In addition to conducting a survey among sites regarding COVID-19 practice changes, the sponsor provided study sites with a memorandum on March 24, 2020 outlining study management requirements in light of the COVID-19 public health emergency and to stress the importance of following national and local practices in the best interest of the patients, research staff at the clinical sites, and Contract Research Organization employees (Appendix 16.1.1). At the time, follow-up for the primary endpoint was complete for nearly all patients, and all sites were instructed to notify the sponsor and IRB/EC prior to implementing any changes in monitoring or testing for the primary endpoint. The electronic case report forms (eCRFs) were modified to collect information about whether alternative

methods were used and to consistently track assessments that were missed due to the COVID-19 pandemic.

As shown in Table 10, by March 15, 2020, approximately 85% of the study patients had completed their evaluation period for the secondary endpoints. Thus, only a limited number of study patients were at risk for any potential impact of COVID-19 on the evaluation of the study secondary endpoints. In addition, these patients were similarly distributed between the two study arms.

Based on the survey responses and the data in Table 10, the study sponsor and principal study statistician determined that the planned analyses for the study endpoints do not need to be changed from the pre-determined plan described in the study's SAP. A description of the procedures, results, and conclusions described in this section was assembled into a SAP addendum and submitted to regulatory authorities.

Table 10: Number of Randomized Patients with Endpoint Evaluation Period Completed Prior to March 15, 2020

		Randomized to Omidubicel (N=62)		Randomized to UCBU (N=63)	
Endpoint	**Criteria Met before March 15, 2020**	**n**	**%**	**n**	**%**
First Grade 2/3 bacterial or Grade 3 fungal infection by Day 100 post-transplant	Enrolled for 100 Days post-transplant if transplanted by Day 90, enrolled for 130 Days post randomization if not transplanted by Day 90 post randomization, or had an event/competing risk/censoring	53	85.5	57	90.5
Number of days alive and out of hospital in the first 100 Days post-transplant	Enrolled for 100 Days post-transplant if transplanted by Day 90, not transplanted by Day 90 post randomization, died, or no longer followed	52	83.9	55	87.3
Platelet engraftment by Day 42 post-transplant	Enrolled for 42 Days post-transplant if transplanted by Day 90, not transplanted by Day 90 post randomization, or had an event/competing risk/censoring	56	90.3	60	95.2
NRM by Day 210 post randomization	Enrolled for 210 Days post randomization, or had an event/competing risk/censoring	47	75.8	47	74.6

Data Source: Appendix 16.2.4.11
N=Total number of patients in each treatment group; n= Number of patients by endpoint for each treatment group.
Abbreviations: NRM: Non-relapse mortality; UCBU: Unmanipulated cord blood unit

9.8.3 Changes in the Planned Analyses

There were five versions of the SAP. A summary of the principal changes in the planned analyses is outlined below. Specifics of all SAP changes can be found in Section 14 of the SAP version 5.0 (Appendix 16.1.9). Other clarifications on the analyses are provided in memos found in Appendix 16.1.9. All changes to the SAP were made by the principal statistician who remained blinded to the data throughout the study until data lock. With the exception of the SAP COVID-19 amendment, all changes were made prior to the first

analysis of data. The SAP COVID-19 amendment was incorporated following the analysis of neutrophil engraftment and prior to the analysis of all other endpoints.

SAP version 2.0 (25 August 2017);

- Changes following FDA guidance:
- NRM by 210 days post-transplant was changed to a tertiary endpoint and endpoints listed as "other secondary" were changed to exploratory endpoints in line with the same protocol changes per recommendation from FDA.
- Gender, race/ethnicity, and geographic region added as planned subgroup analyses.
- Plan to use Hommel's method for multiple comparison p-value adjustment rather than Benjamini Hochberg.
- Rerandomization method for determining confidence intervals described and specified as additional method for the primary and secondary endpoint analyses.
- Added a secondary analysis of the primary endpoint to compare time to neutrophil engraftment using the LogRank test statistic in the ITT population.
- Clarified that relapse prior to transplant is not counted as an event or competing risk unless there is a failure to be transplanted within 90 Days following randomization.
- Specified procedures for handling missing HRQoL data.

SAP version 3.0 (09 January 2018):

- An additional secondary analysis of the primary endpoint was added to adjust for any imbalance in disease type
- Specified chimerism for engraftment can be obtained at any time after ANC recovery up to Day 100 post-transplant instead of just the first measurement post-transplant

SAP version 4.0 (19 December 2019):

- Added that the AT population would not include patients who received a transplant product that was Out of Specification (OOS).
- Specified procedure for calculating rerandomization distribution when minimization factors used in randomization are changed after randomization for a patient.
- A supplemental analysis of the primary endpoint added to compare the time to ANC recovery in the ITT population.
- Added specifics for analyses of treatment-emergent AEs and maximum severity of AEs.

SAP version 5.0 (08 March 2020)

- Specified rerandomization tests were limited to ITT analyses and Mann-Whitney/Wilcoxon Rank Sum test or asymptotic test for non-ITT analyses of primary and secondary endpoints.
- Added secondary analyses for exploratory endpoint of Day 16 neutrophil engraftment in the transplanted population (TP) and AT populations.

- Test for some exploratory endpoints changed from rerandomization to other tests as applicable.
- Added AT analysis to exploratory endpoint of neutrophil engraftment failure by 42 days and changed test from rerandomization to Fisher's test for difference in proportions.
- Addendum for changes related to the COVID-19 public health emergency added on August 31, 2020.

SAP memos and clarifications

The following memos were created prior to the September 8, 2020 data lock in order to clarify methods described in the SAP. These memos are provided in Appendix 16.1.9:

- **Statistical Method Equivalence -** This memo demonstrates the equivalence of the Mann-Whitney test statistic and the Gehan-Wilcoxon with competing risks test statistic when there are no losses to follow-up. This pertains to the methods related to the analysis for the primary endpoint of neutrophil engraftment.

  PSHREG macro - This memo provides detail on using the PSHREG macro for the competing risk analysis of neutrophil engraftment in the event of loss to follow-up before Day 42
  Confidence Interval for Difference in Medians - This memo provides details for calculation of the confidence interval for the difference in median time to engraftment when there is censoring and/or competing risks.
  Cumulative Incidence - This memo specifies that, in addition to the analyses specified in the SAP, a calculation for within-treatment group median time to neutrophil engraftment and bootstrap confidences for these median times will be provided for neutrophil engraftment and the within-group confidence intervals may be provided for platelet engraftment.
  Populations Definitions - This memo clarifies the definition of the ANC-engrafted population (AEP) and the platelets-engraftment population (PEP).
  Rerandomization Confidence Intervals - This memo updates the formula for the calculation of the rerandomization confidence intervals.
  Primary Analysis Method - The SAP describes two methods of analysis for the primary endpoint of neutrophil engraftment; the first method is the P statistic based on the Mann-Whitney statistic and would be used if there is no missing data for the primary endpoint, and the second method is the "Gehan-Wilcoxon" approach based on the average hazard ratio statistic and would be used if there were missing data for the primary endpoint. This memo documents that the primary analysis of neutrophil engraftment will use the method that utilizes the statistic P based on the Mann-Whitney statistic.

For the analysis of total number of days alive and out of hospital, the SAP describes calculating the p-value based on the rerandomization of the Mann-Whitney U statistic and using the P statistic for rerandomization and bootstrap confidence intervals. However, the actual method used for calculating the p-value was the same as for the primary endpoint

based on the P statistic because it is equivalent to using the method based on the Mann-Whitney.

Analysis timepoints and data locks

Study data were analyzed, and results presented to the study sponsor based on three separate data locks; May 7, 2020, September 8, 2020, and April 29, 2021. These three analysis timepoints were pre-specified in Section 10.4.1 of the study protocol (Appendix 16.1.1).

Following the May 7, 2020 data lock, results of the primary endpoint, time to neutrophil engraftment, were analyzed and reported along with baseline demographics, patient disposition, and other exploratory endpoints related to neutrophil engraftment. None of the secondary endpoints or other exploratory endpoints were analyzed or reported at that time and sponsor blinding was maintained to these other outcomes.

All endpoints were analyzed following the September 8, 2020 data lock. At that time all patients had completed 210 days of follow-up following randomization (or 180 days following transplant) and the majority had completed the study. Following the data lock, the study sponsor was unblinded to all individual patient data. The original intent was to use this data as the basis for the final Clinical Study Report (CSR) and license application to Regulatory Authorities. However, after further consultation with Regulatory Authorities, it was determined that the license application would be delayed in order to accumulate more data from the manufacturing facility intended for post licensure production.

The April 29, 2021 data lock included all patient's follow-up data through completion of the study. This data lock was originally intended to provide re-analysis of the exploratory endpoints at 1 year post-transplant and 15 months post-randomization. However, given the unplanned delay in submission of the license application, it was decided to use this final data lock as the basis for the results presented in the CSR.

Data updated between September 8, 2020 and April 29, 2021 did not impact the interpretation of any of the primary or secondary analyses. The majority of changes between these two data locks represented the addition of data following new patient visits after September 8, 2020. There were also some data entry error corrections that were included in the final data lock.

Table 14.2.1.10.1 summarizes the changes in the primary, secondary, and tertiary endpoints, except for days alive and out of hospital.

There were no changes related to neutrophil engraftment or platelet engraftment by Day 42.

There were three changes related to the endpoint for bacterial infections Grade 2/3 or invasive fungal infections by Day 100. All three changes involved corrections of data entry errors from the previous data lock, namely the identification of previously unreported infections; one omidubicel patient changed from competing risk at Day 31 to an infection at Day 23, one unmanipulated CBU patient changed from censor at Day 160 to infection at Day 1, and one unmanipulated CBU patient changed from infection at Day 143 to infection at Day 95. As a result of these three changes, the difference in cumulative incidence between the two groups changed from –0.20 (95% CI –0.35 to –0.03, p=0.027) in favor of omidubicel to –0.22 (95% CI –0.38 to –0.03, p=0.016) in favor of omidubicel.

There was one change related to the endpoint for NRM by Day 210 post-randomization. This change was related to additional follow-up that moved a patient's censor time from Day 210 to after Day 210. This change did not affect the results of the analysis of NRM by Day 210.

Table 14.2.3.5.1 summarizes the changes related to the secondary endpoint of days alive and out of hospital. There was one change for this endpoint due to correction of a data entry error from the previous data lock; a patient's discharge date was corrected which changed their total days alive and out of hospital from 33 to 31 days. This change had no impact on the probability of more days alive and out of hospital or the associated p-value.

Table 14.3.10.1 summarizes changes related to AEs. There was a total of 28 new or modified AE records. Two of these changes were new events due to additional follow-up. Twenty-six changes were related to corrections of data entry errors; three event not previously reported, 16 events removed from four patients in the unmanipulated CBU arm, three changes in event grading, two non-SAEs (Grade 3 mucosal inflammation and Grade 3 pain for one patient) changed causality from related to omidubicel to unrelated, and two events changed causality from not applicable (pre-transplant event) to not related. None of these changes impacted the overall safety profile of omidubicel.

Table 14.1.12.4 summarizes changes related to a range of baseline patient characteristics and follow-up status, including survival, relapse, and occurrence of infusion reactions. There were no changes related to baseline patient characteristics. There were four new deaths reported due to additional follow-up and two changes due to data entry errors; two unmanipulated CBU patients had changes related to occurrence of infusion reactions.

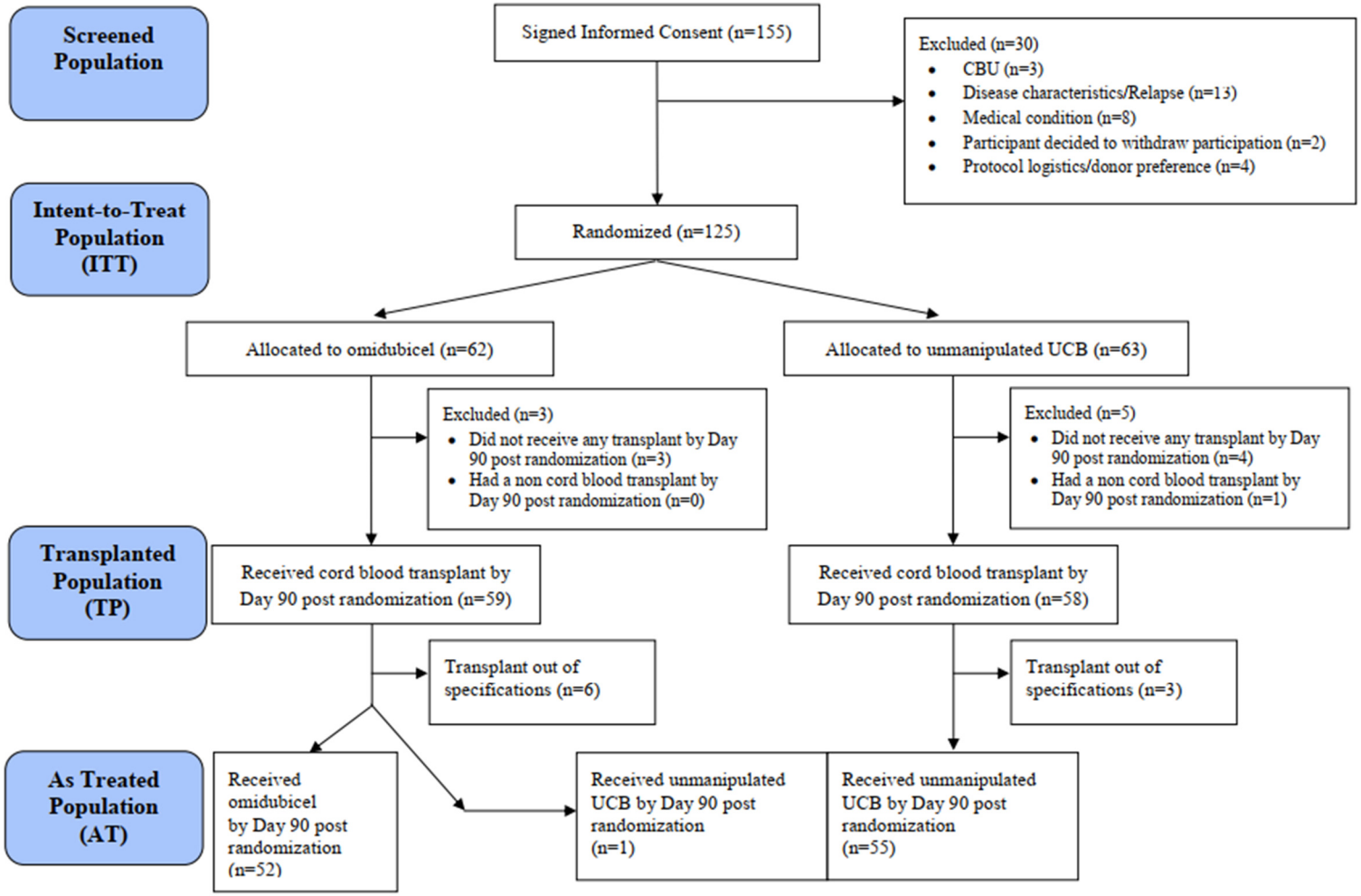
10 STUDY PATIENTS

During this study, patients were enrolled across 33 sites globally. First consent was provided on December 20, 2016 and first patient was randomized on January 09, 2017. The last patient visit was April 15, 2021. The cutoff date for this analysis was April 29, 2021.

10.1 Disposition of Patients

A schematic of the overall disposition of study patients is presented in Figure 2. Of the 155 patients who provided consent, 125 were randomized, while 30 were considered screen failures due to disease characteristics or relapse (n=13), medical condition (n=8), protocol logistics/donor preference (n=4), CBU selection considerations (n=3), and/or voluntary withdrawal (n=2).

Figure 2: Study Flow Diagram



Data Source: Figure 14.1.1

n= Number of patients in each defined group

Abbreviations: CBU: Cord blood unit; UCB: umbilical cord blood

Table 11: Patients in ITT Population Excluded from Transplant Population

Excluded from TP	Randomized Treatment Group	Patient ID	Reason Classified	Specified Reason
Did not receive any transplant by Day 90 post randomization	Omidubicel	GP3DUK-002	Relapse	Relapsed disease
Did not receive any transplant by Day 90 post randomization	Omidubicel	GP3KMC-004	Medical condition	Consolidation therapy due to MRD+ finding followed by sinus infection
Did not receive any transplant by Day 90 post randomization	Omidubicel	GP3RCI-001	Relapse	Relapsed disease
Did not receive any transplant by Day 90 post randomization	UCBU	GP3CCF-003	Relapse	Relapsed disease
Did not receive any transplant by Day 90 post randomization	UCBU	GP3CCF-005	Relapse	Relapsed disease
Did not receive any transplant by Day 90 post randomization	UCBU	GP3LAF-002	Relapse	AML relapse and refractory
Did not receive any transplant by Day 90 post randomization	UCBU	GP3OHS-006	Medical condition	Delayed transplant- too necrotic in BM and MRD+
Had a non-cord blood transplant by Day 90 post randomization	UCBU	GP3DFC-007	Investigator Decision	Received a mismatched unrelated donor transplant due to concerns for liver toxicity

Data Source: Table 14.1.2.1

Abbreviations: AML: Acute myelogenous leukemia; BM: Bone marrow; MRD: Minimal residual disease; TP: Transplanted population; UCBU: Unmanipulated cord blood unit

Table 12: Patients in Transplanted Population and Excluded from As-Treated Population

Excluded from AT Population	Randomized Treatment Group	Treatment Received	Patient ID	Reason
Investigator decision to pursue a different transplant / CBU does not meet protocol requirements	Omidubicel	UCBU	GP3LAF-008	Due to issues with shipping the selected CBU to the Production facility, the physician investigators determined the patient could not wait for omidubicel production for study transplant. Per PI discretion, patient was removed from study-specific procedures. A single CBU was transplanted but it did not meet criteria for single cord transplant. HLA match was 4/6 and CD34 dose was 1.3×10^5 cells/kg
Product OOS / CBU does not meet protocol requirements	Omidubicel	UCBU	GP3RMH-001	The patient was randomized to receive omidubicel but was infused with a double unmanipulated CBU infusion instead. The unit sent for production had a harvest TNCC below specification (4.2×10^8 cells). Processed unit was discarded, and physician investigator decided the patient could not wait for another production cycle to receive transplant. Patient received double cord transplant but neither unit met protocol criteria. Unit 1 TNCC was 1.40×10^9 and Unit2 CD34 count was 7.08×10^6.
Investigator decision to pursue a different transplant / CBU does not meet protocol requirements	Omidubicel	UCBU	GP3UMN-008	The treating physician decided the patient was not suitable to be a research study patient (patient was consented by a different physician as the treating physician was out of town at the time of consent). Patient removed from study-specific procedures. Patient received a double CBU transplant per standard of care at UMN. Given single cord transplant that did not meet protocol criteria. HLA match was 4/6 and CD34 dose was 0.9×10^5/kg and TNC dose was 2.8×10^7/kg
Product OOS	Omidubicel	Omidubicel	GP3DFC-006	After the harvest of omidubicel CF, it was determined that the total number of viable cells (TNC) was 6.7×10^8 cells. Per the protocol, the TNC for the final omidubicel CF must be $\geq 8.0 \times 10^8$ cells. The product met all other FPQC tests and release criteria. The FDA approved transplantation of this OOS product.

Excluded from AT Population	Randomized Treatment Group	Treatment Received	Patient ID	Reason
Product OOS	Omidubicel	Omidubicel	GP3NWU-002	After the harvest of omidubicel CF, it was determined that the total number of viable cells (TNC) was 6.5×10^8 cells. Per the protocol, the TNC for the final omidubicel CF must be $\geq 8.0 \times 10^8$ cells. The product met all other FPQC tests and release criteria. The FDA approved transplantation of this OOS product.
Product OOS	Omidubicel	Omidubicel	GP3OHS-005	After the harvest of omidubicel CF, it was determined that the total number of viable cells (TNC) was 5.2×10^8 cells. Per the protocol, the TNC for the final omidubicel CF must be $\geq 8.0 \times 10^8$ cells. The product met all other FPQC tests and release criteria. The FDA approved the transplantation of this OOS product.
CBU does not meet protocol requirements	UCBU	UCBU	GP3CCF-004	Patient should have received double cord but received single instead. HLA match was 4/6 and Unit 1 CD34 dose was 1.4×10^5/kg. This was site error and is recorded as a protocol deviation.
CBU does not meet protocol requirements	UCBU	UCBU	GP3KMC-002	CBU1 was replaced because original cord was unavailable. Neither cord of the double cord transplant met TNCC criteria of $\geq 1.8 \times 10^9$. Unit 1 TNCC was 1.36×10^9 and Unit 2 TNCC was 1.51×10^9.
CBU does not meet protocol requirements	UCBU	UCBU	GP3UMN-009	Post thaw testing revealed CBU1 had 60% viability. CBU replaced but neither CBU infused met protocol criteria. Unit1 TNCC was 1.62×10^9 and Unit 2 CD34 count was 3.50×10^6 and Unit 2 TNCC was 1.698×10^9.

Data Source: Listing 16.2.4.5

Abbreviations: AT: As-treated; CBU: Cord blood unit; CF: Cultured fraction; FPQC: Final process quality controls; HLA: Human leukocyte antigen; OOS: Out of specification; PI: Principal investigator; TNCC: Total nucleated cell count; UCBU: Unmanipulated cord blood unit; UMN: University of Minnesota

Table 13: Patients in As-Treated Population Who Received Unmanipulated CBU Instead of omidubicel

Randomized Treatment Group	Treatment Received	Patient ID	Reason
omidubicel	UCBU	GP3SGH-004	Initial unit sent for production had a TNCC below specification. Processed unit was discarded, and a second unit was selected for shipment. The second unit sent was found to have a CFU count OOS. The processed unit was discarded, and physician investigator decided the patient could not wait for another production cycle to receive transplant. The patient was transplanted with UCBU.

Data Source: Listing 16.2.4.3
Abbreviations: CFU: Colony forming units; OOS: Out of specification; TNCC: Total nucleated cell count; UCBU: Unmanipulated cord blood unit

Of the 125 enrolled patients, 62 patients were randomized to the omidubicel treatment group, and 63 patients were randomized to the unmanipulated CBU group. Collectively, this comprised the ITT population (Table 14.1.2). Patients randomized to omidubicel were transplanted within a median 42 days (range 16-90), compared to 26 days (range 15-89) for the unmanipulated CBU group (Table 14.1.17.2).

The TP comprised 59 patients in the omidubicel treatment group and 58 patients in the unmanipulated CBU group. Eight patients in the ITT population were excluded from the TP because they did not receive either omidubicel or unmanipulated CBU within 90 days following randomization (Table 14.1.2.1). Three patients from the omidubicel treatment group and five patients from the unmanipulated CBU treatment group were excluded. The most frequent reason was relapse – two patients on the omidubicel arm and three patients on the unmanipulated CBU arm relapsed prior to transplantation and were not able to receive a transplant within 90 days of randomization (Table 14.1.2.2).

The omidubicel AT population comprised 52 patients randomized to and treated with omidubicel. The unmanipulated CBU AT population comprised 56 patients: 55 randomized to and treated with unmanipulated CBU, and one patient randomized to omidubicel who received unmanipulated CBU (Table 14.1.4). This patient (GP3SGH-004) was randomized to omidubicel but was transplanted with unmanipulated CBU because of a manufacturing failure (Table 14.1.4.1). Nine patients in the TP were excluded from the AT population because they received a graft that was not within specifications (Table 14.1.3.1). Six patients randomized to the omidubicel treatment group were excluded from the AT population; three received an OOS omidubicel product, and three received an unmanipulated CBU that did not meet protocol-specified criteria for CBU selection (Table 14.1.3.2).

In total, ten patients randomized to omidubicel and eight patients randomized to unmanipulated CBU were not transplanted per protocol. Of these patients, 5 patients on each arm (8%) did not receive a transplantation within the protocol-defined timelines, or received a transplantation with a different graft source, due to their disease status (disease relapse) or a medical condition precluding their transplantation, or because the study investigator decided to pursue a different treatment option. In addition to these five patients, on the unmanipulated CBU arm three patients were transplanted with CBUs that did not meet the protocol-defined CBU requirements, as a result of safety or logistic issues that precluded the use of their original intended CBUs. On the omidubicel arm, five patients (8%) could not receive omidubicel according to the protocol specifications due to production failures. Three of these patients received omidubicel that did not meet product specifications under FDA approval, and two patients were transplanted with backup CBUs.

Two patients withdrew consent for further follow-up prior to study completion. One patient withdrew consent after 210 days post-randomization (patient was not transplanted), and the other patient was withdrawn from the study after one year post-transplant but prior to Month 15 post-randomization due to patient lack of compliance issues and patient relocation (Listing 16.2.1.1). All other patients were followed until completion of month 15 follow-up or death. Median follow-up for ITT patients was 422.5 days for the omidubicel arm and 429.0 days for the unmanipulated CBU arm (Table 14.1.11).

In addition to the two patients who withdrew consent for further follow-up, six patients were withdrawn from study-specific procedures but did not withdraw consent for further collection of standard of care follow-up information. Patient information and reasons for withdrawal from study-specific procedures are provided in Listing 16.2.1.1.

Patient disposition by country and screening site is presented in Table 14.1.8. Randomization assignments were well-balanced across geographical regions. Specifically, a total of 109 patients were consented and screened in the United States with 87 randomized, 42 to omidubicel and 45 to unmanipulated CBU. In Spain, 15 patients were randomized, eight to omidubicel and seven to unmanipulated CBU. Patients were also randomized in Singapore (N=9), The Netherlands (N=6), Brazil (N=4), Israel (N=2), and the United Kingdom (N=2). Across all geographies, nine clinical sites randomized at least six patients each (range 6-14); 12 clinical sites randomized 2-4 patients each; 12 clinical sites randomized one patient each.

10.2 Protocol Deviations

Protocol deviations were classified as minor, major, or critical, as defined in the study monitoring plan.

Major protocol deviations (MPDs) included issues that potentially impact the integrity of the study or patient treatments such as patient consenting, patient eligibility or the administration of the study treatments (Listing 16.2.2.2). These included violations in the administration of the allocated graft, or the dosing of the conditioning regimen, G-CSF or mandatory prophylaxis regimens. Other protocol deviations were classified as minor protocol deviations (mpds) (Listing 16.2.2.3).

Throughout the study, a total of 61 MPDs and 740 mpds were reported for a total of 115/125 (94%) randomized patients. No critical deviations were reported.

In addition, a total of two MPDs and four mpds were reported among the 30 patients who consented but were screen failures. These deviations were either related to informed consent procedures (two MPDs) or failure to record the patient in the EDC within the required timelines from ICF signature (4 mpds). These deviations were not included in the general summary and analysis.

An average of 0.5 MPDs and 5.9 mpds were reported per randomized patient. The geographic distribution of deviations is outlined in Table 14.

Table 14: Major and Minor Protocol Deviations by Geographic Region (ITT Population; N=125)

Region	Patients (n)	MPD (n)	MPD/ Patient	mpd (n)	mpd/ patient
All regions	125	61	0.5	740	5.9
U.S.	87	35	0.4	369	4.2
Europe (Netherlands, Spain, UK)	23	20	0.9	290	12.6
RoW (Brazil, Israel, Singapore)	15	6	0.4	81	5.4

Data Source: Listing 16.2.2.2, Listing 16.2.2.3
n= Number of patients or number of deviations per region from the ITT Population
Abbreviations: ITT: Intent-to-treat population; MPD: Major protocol deviation; mpd: Minor protocol deviation; RoW: Rest of the world

The sites with the highest proportion of deviations recorded were summarized below, however as can be seen these were primarily due to small numbers of patients with an excess of deviations.

The sites with the highest number of MPDs per randomized patients were the following:

- UTR01 (two patients): 2.5 MPDs/patient
- VAL01(three patients): 2.3 MPDs/patient
- RMH01 (one patient): 2.0 MPDs/patient
- HSP01 (one patient), DCH01 (two patients), UTN01 (two patients) and CAL01 (two patients): One MPD/patient

The sites with the highest number of mpds per randomized patients were the following:

- UTR01 (two patients): 25.5 mpds/patient
- RAB01 (one patient): 18 mpds/patient
- VAL01 (three patients): 15.3 mpds/patient
- HSP01 (one patient): 14 mpds/patient
- HFM01 (one patient) and CMC01 (one patient): 13 mpds/patient

The study teams at the sites were re-trained as necessary to avoid recurrence of deviations, and reporting to the local authorities (EC/IRB and/or competent authorities) was performed as required.

Study deviations were reviewed on an ongoing basis by the Sponsor to identify recurring areas of non-compliance that could be resolved by removing or modifying the relevant requirements in subsequent protocol amendments. A total of 55 deviations were addressed as such, including three (5.5%) MPDs and 52 (94.5%) mpds (Listing 16.2.2.10).

10.2.1 Changes in Research

Protocol deviations that were pre-approved by IRB/FDA (and Sponsor when applicable) were categorized as “changes in research” (Listing 16.2.2.11). The classification as minor or major did not apply to this category. A total of eight changes in research were documented,

all granted in the US: three patients received approval to be infused with omidubicel that did not meet product specifications; three changes in research were related to eligibility assessments performed out-of-window or with a result out-of-window; one change in research was related to a change in dose of conditioning regimen and one change in research was related to the use of a sample initially drawn for immune reconstitution, to assess the chimerism component required for the primary endpoint.

10.2.2 Deviations Related to the Covid-19 Public Health Emergency

With the emergence of the Covid-19 world health emergency, specific deviations were flagged as related to the constraints inflicted by the pandemic (Listing 16.2.2.4). A total of 83 such deviations were reported in 26 patients, in addition to those outlined in Table 14.

All these deviations were mpds. Four of them were informed consent deviations while 79 were related to missed assessments or assessments performed out-of-window. The deviations were not considered to have a major impact on the outcomes of the study.

Table 15 provides a summary of deviations by type.

Table 15: Deviations Type and Assigned Treatment (ITT Population; N=125)

	Omidubicel Arm N=62		UCBU Arm N=63	
	Deviations (n)	**Patients (n, %)**	**Deviations (n)**	**Patients (n, %)**
Minor protocol deviations[a]	370	59 (95.2%)	370	56 (88.9%)
Minor deviations addressed in subsequent protocol amendments	32	13 (21.0%)	20	12 (19%)
Major protocol deviations[a]	34	25 (40.3%)	27	23 (36.5%)
Major deviations addressed in subsequent protocol amendments	2	2 (3.2%)	1	1 (1.6%)
Changes in research	5	5 (8.1%)	3	3 (4.8%)
Covid-19 related deviations	33	14 (22.6%)	50	12 (19.0%)

Data Source: Listing 16.2.2.2, Listing 16.2.2.3, Listing 16.2.2.4, Listing 16.2.2.11
N= Total number of patients per treatment arm from the ITT Population; n= Number of deviations or patients per deviation category for each treatment arm
[a] Not including Covid-19 related deviations or changes in research
Abbreviations: ITT: Intent-to-treat; UCBU: Unmanipulated cord blood unit

The study deviations were classified in nine specific categories and two more general ones (Summarized in Table 16). The majority of deviations were reported as “Other protocol procedure or assessment”, encompassing 487 deviations in 104 patients (11 MPDs and 476 mpds). These included primarily assessments that were missed or performed outside of the protocol allowed time window. Among the specific categories, 145 deviations in screening assessments or procedures were reported in 67 patients (five MPDs and 140 mpds). A summary of the deviations by categories and assigned treatment arm is shown in Table 16. Those deviations do not include Covid-19 related deviations or changes in research.

Table 16: Deviations by Category and Assigned Treatment Arm (ITT Population; N=125)

	Omidubicel Arm N=62		UCBU Arm N=63	
	Deviations (n)	**Patients (n,%)**	**Deviations (n)**	**Patients (n,%)**
All Categories[a]	403	59 (95.2%)	398	56 (88.9%)
Eligibility criteria violation	2	2 (3.2%)	2	2 (3.2%)
Informed consent	5	5 (8.1%)	5	4 (6.3%)
Infusion day[b]	40	27 (43.5%)	20	16 (25.4%)
Other	5	5 (8.1%)	1	1 (1.6%)
Other protocol and procedure assessment	228	53 (85.5%)	259	51 (81.0%)
Received excluded concomitant medication	0	NA	1	1 (1.6%)
Received non-randomized/OOS product	0	NA	1	1 (1.6%)
Reporting timelines	25	17 (27.4%)	24	17 (27.0%)
Safety	2	2 (3.2%)	0	NA
Screening assessment or procedure	79	35 (56.5%)	66	32 (50.8%)
Study medication and administration	16	14 (22.6%)	20	15 (23.8%)

Data Source: Listing 16.2.2.2, Listing 16.2.2.3

N= Total number of patients per treatment arm from the ITT Population; n= Number of deviations or patients per deviation category for each treatment arm

[a] Not including Covid-19 related deviations and changes in research

[b] For Infusion day deviations, the data is provided according to the treatment actually received rather than the randomized treatment – Omidubicel (N=52) and UCBU (N=56)

Abbreviations: OOS: Out of specifications; UCBU: Unmanipulated cord blood unit

A total of nine MPDs and 51 mpds were reported as infusion day deviations in patients treated with either omidubicel or unmanipulated CBU. Most frequently, infusion day deviations were related to the dosing of pre-medications administered as infusion support (19 deviations in omidubicel patients and 16 deviations in unmanipulated CBU patients). Among the patients treated with omidubicel, ten deviations were reported for temperature excursions during storage or shipment and six deviations were related to the infusion not performed per protocol. Only two such deviations were reported for the unmanipulated CBU patients.

This difference was expected, since omidubicel was an experimental treatment that the centers had less experience with compared to the standard of care for those who received unmanipulated CBU. Omidubicel infusion required closer scrutiny to ensure correct utilization and patient safety and was therefore also associated with more deviations.

Deviations related to the infusion of omidubicel were specifically assessed for any impact on patient outcomes following transplantation. Infusion reactions, time to neutrophil engraftment, and days alive and out of hospital within 100 Days post-transplant were similar among patients with or without such deviations.

All temperature excursions during storage or internal shipment that were reported as deviations were assessed by the Sponsor during the course of the study and determined to be acceptable in terms of product safety.

In conclusion, protocol deviations appeared to be balanced between study arms except for infusion day deviations which were predictably more on the omidubicel arm. The deviations observed are not believed to have impacted patient safety, the overall data quality of the study, or the interpretation of the analysis results.

11 EFFICACY EVALUATION

11.1 Data Sets Analyzed

The efficacy analyses presented in this report reflect data accumulated as of the cutoff date, April 29, 2021.

All randomized patients (N=125) were included in the ITT population, which was used for the primary analysis of the primary, secondary, tertiary, and most of the exploratory endpoints. There were no patients excluded from this population nor from any of these analyses. Other populations used for analysis were pre-specified in the protocol and included the TP, the AT, the AEP, the Platelets Engrafted population (PEP), and Safety population (SP). Details regarding patients excluded from these populations are discussed in Section 10.1.

The TP comprised all patients who received omidubicel or unmanipulated CBU and provided the primary analyses for the exploratory endpoints that depend on transplant, such as GvHD, duration of primary hospitalization, and secondary graft failure. Similar to the ITT population, these patients were retained in the treatment group to which they were assigned regardless of the type of transplant received. For example, a patient who was randomized to omidubicel but received unmanipulated CBU was still considered part of the omidubicel group in the TP.

The AT population comprised all randomized patients who received omidubicel or unmanipulated CBU transplant within specifications and were grouped by the treatment performed. Patients were excluded from the omidubicel AT population if they received omidubicel that was not within product specifications or if they received unmanipulated CBU. Patients were excluded from the unmanipulated CBU AT population if they received unmanipulated CBU that did not meet the protocol specific criteria for CBU selection. Analysis of the AT population is for supportive purposes, to describe the activity in patients treated with omidubicel compared to patients treated with unmanipulated cord blood and did not serve as the primary analysis for any of the efficacy endpoints. The decision to exclude patients who did not receive a transplant within specifications was made in SAP Amendment 4, prior to the completion of enrollment.

The AEP comprised patients who achieved neutrophil engraftment and provided supportive analyses for time to neutrophil engraftment.

The PEP comprised patients who achieved platelet engraftment and was the primary analysis for the exploratory endpoint of time from transplant to platelet engraftment.

The SP is the same population as the AT population and provided the basis for analyses on the safety and tolerability of omidubicel transplantation.

11.2 Demographic and Other Baseline Characteristics

Categorical demographic and baseline characteristics of the ITT population are presented in Table 14.1.12 and continuous characteristics are presented in Table 14.1.12.1. Patient demographics for the AT population are presented in Table 14.1.12.2.

Table 17: Main Demographics and Baseline Characteristics (ITT Population)

	Randomized Treatment Group	
	Omidubicel (n, %)	**UCBU (n, %)**
Total randomized[a]	62 (100.0%)	63 (100.0%)
Gender		
Female	30 (48.4%)	23 (36.5%)
Male	32 (51.6%)	40 (63.5%)
Age (years)		
12-39	31 (50.0%)	29 (46.0%)
40-59	27 (43.5%)	31 (49.2%)
60-65	4 (6.5%)	3 (4.8%)
Race		
White	35 (56.5%)	37 (58.7%)
Black	11 (17.7%)	9 (14.3%)
Asian	7 (11.3%)	10 (15.9%)
Unknown/Other/Missing or more than one race	9 (14.5%)	7 (11.1%)
Ethnicity		
Hispanic or Latino	10 (16.1%)	6 (9.5%)
HCT-specific Comorbidity Index		
0	12 (19.4%)	14 (22.2%)
1-2	19 (30.6%)	16 (25.4%)
3+	31 (50.0%)	33 (52.4%)
Primary diagnosis		
AML	27 (43.5%)	33 (52.4%)
ALL	20 (32.3%)	21 (33.3%)
MDS	6 (9.7%)	3 (4.8%)
CML	4 (6.5%)	2 (3.2%)
Lymphoma	3 (4.8%)	2 (3.2%)
Other rare disease	2 (3.2%)	2 (3.2%)
Disease risk group		
Low	15 (24.2%)	15 (23.8%)
Moderate	27 (43.5%)	25 (39.7%)
High/Very High	20 (32.3%)	23 (36.5%)
Intended cord blood transplant		
Single	20 (32.3%)	21 (33.3%)
Double	42 (67.7%)	42 (66.7%)
Antigen-level HLA match score (Intended Treatment CBU #1)		
4/6	46 (74.2%)	46 (73.0%)
5/6	15 (24.2%)	16 (25.4%)
6/6	1 (1.6%)	1 (1.6%)

Data Source: Listing 16.2.4.1

[a] Site, age at randomization, intent for single or double cord transplantation, and disease risk group are the factors used in the minimization algorithm.

Abbreviations: ALL: Acute lymphoblastic leukemia; AML: Acute myelogenous leukemia; CBU: Cord blood unit; CML: Chronic myelogenous leukemia; HCT: Hematopoietic cell transplantation; HLA: Human leukocyte antigen; ITT: Intent-to-treat; MDS: Myelodysplastic syndrome; UCBU: Unmanipulated cord blood unit

As summarized in Table 17, demographics and baseline disease characteristics were well-balanced in the two arms, specifically for those factors used for minimization, and were similarly distributed across the ITT and AT populations. The median age of patients in the study was 40 years for the omidubicel arm and 43 years for the unmanipulated CBU arm. Of note, the study population was ethnically diverse, with over 40% identified as non-Caucasian. Acute leukemias (AML and ALL) were the most common indications for transplant, and most patients had moderate to high-risk disease. Patient ages ranged from 13 to 65 years, and patients with weights up to over 130 kg were enrolled in both arms, reflecting a study population that is representative of the general population eligible for transplant.

Eligible CBUs for the study were required to meet HLA match and cellular requirements. All CBUs were required to be HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high-resolution) loci with the patient. As anticipated, most patients received CBUs that were HLA-mismatched at two loci, reflecting the utility of CBT as a mismatched unrelated stem cell source. Graft characteristics are discussed in Section 11.4.10.

11.3 Measurements of Treatment Compliance

All treatments administered were recorded in the CRF and are presented by patient in Appendix 16.3.2. All doses of the study treatment were administered at the study clinical sites by qualified staff. As the treatment is a single dose transplant administered by clinical site staff, there were no issues with compliance. Patients unable to receive a transplant and those who received fewer cells than required per protocol or per release criteria are detailed in Section 10.1 of this report and were not included in analyses specific to the AT population but were included in all ITT analyses.

All patients who received omidubicel received the full dose. One patient who received unmanipulated CBU (GP3SGH-002) did not receive the entire dose. This subject received a double unmanipulated CBU infusion. Towards the end of the first CBU infusion, the subject developed abdominal pain, intense headache and was hypertensive. Infusion was withheld and decision made to discard the remaining product in tubing (estimated 20 mL) and infusion of the second CBU unit was postponed to the following day. The second CBU infusion was completed the following day with a temporary interruption due to headache. The patient subsequently developed primary graft failure. Details of this patient's medical course are provided in Section 14.3.1.

11.4 Efficacy Results and Tabulations of Individual Patient Data

The efficacy endpoints were designed to provide a robust dataset characterizing the overall risk/benefit of omidubicel transplantation and to assess the clinical benefit. A multiple comparison adjustment of the secondary endpoint analyses was performed using Hommel's method to address family-wise type I error rates.

As detailed in Section 9.5.7.1, the primary efficacy endpoint, time to neutrophil engraftment, was designed to demonstrate the effect of omidubicel in providing rapid neutrophil engraftment in order to address a key barrier to the widespread use of umbilical CB as a graft source. The secondary efficacy endpoints included time to platelet engraftment within 42 days of transplantation, the incidence of Grade 2/3 bacterial or invasive fungal infections by 100 Days, and the number of days alive and out of hospital in the first 100 days following transplantation;

these were designed to assess key milestones occurring in the first weeks to months following transplantation to demonstrate the clinical benefit associated with neutrophil engraftment assessed in the primary endpoint.

Additionally, the tertiary endpoint- NRM by 210 Days following randomization- provides further support for the primary and secondary endpoints, as this timepoint provides approximately 6-months of post-transplant follow-up.

11.4.1 Neutrophil Engraftment

This section includes the efficacy results of three endpoints that assessed neutrophil engraftment:

1. Primary endpoint: Time to neutrophil engraftment following transplantation
2. Exploratory endpoints: Neutrophil engraftment by 16 days and 42 days following transplantation

11.4.1.1 Primary Endpoint: Time to Neutrophil Engraftment Following Transplantation

The study met its primary endpoint, demonstrating by ITT analysis that the time to engraftment was shortened by omidubicel transplantation compared to unmanipulated CBU transplantation ($p<0.001$). The median time to neutrophil engraftment was 12 days (95% CI 10-14) for the omidubicel group, and 22 days (95% CI 19-25) for the unmanipulated CBU group, being shorter in the omidubicel group by 10 days (95% CI 6.4-12.9; rerandomization) (Table 14.2.1.7.2).

The estimated probability that a patient in the omidubicel arm had a shorter engraftment time than a patient in the unmanipulated CBU arm was 0.77 (95% CI 0.66-0.85; rerandomization) (Table 14.2.1.1.2). As shown in Figure 4, 89% of patients in the omidubicel arm achieved successful neutrophil engraftment by 42 days post-transplant, compared to 84% of patients who received unmanipulated CBU. All cumulative incidence curves presented in this report incorporate adjustment for competing risks.

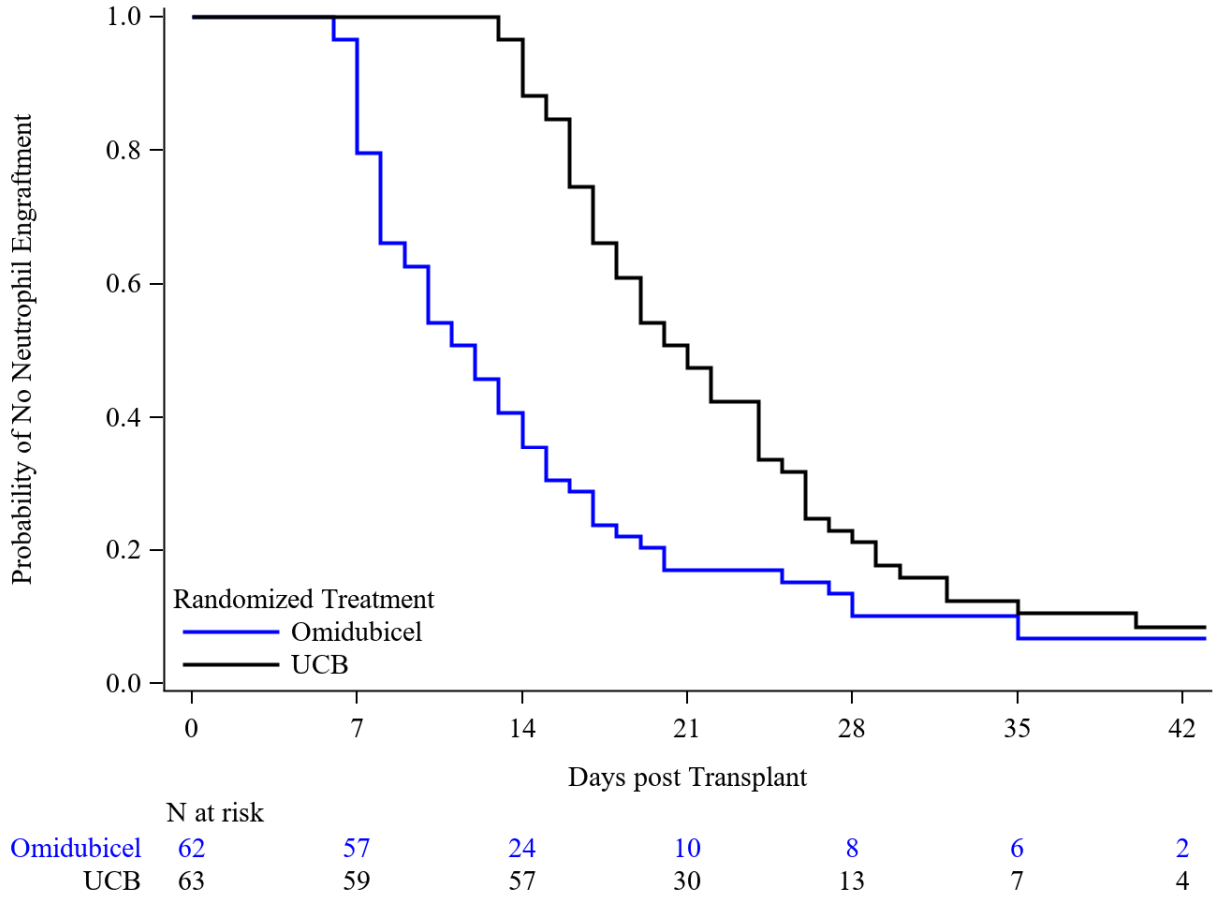
Sensitivity analyses were performed where patients with a competing risk (such as no transplant or relapse before engraftment) were assigned a rank worse than graft failure. The results of the sensitivity analysis were identical to the primary analysis for probability of shorter engraftment and median time to engraftment (Table 14.2.1.2.1). A secondary analysis of the primary endpoint stratified by disease indicated that the difference in time to neutrophil engraftment was still statistically significant ($p<0.001$) when stratified by disease (Table 14.2.1.6.1). The shorter engraftment time for omidubicel ($p<0.001$) was also demonstrated in a secondary analysis where pre-transplant relapse was considered a competing risk (Table 14.2.1.7.2, Table 14.2.1.7.3).

Looking at only ANC recovery without regard to chimerism, median time to recovery was also 12 days (95% CI 10-14) for the omidubicel group and 22 days (95% CI 19-25) for the unmanipulated CBU group, being shorter in the omidubicel group by 10 days (95% CI 6.0-14.0) (Table 14.2.1.9.2).

A secondary analysis using a LogRank test was performed, estimating the probability of engraftment from the point of transplant in the two arms of the ITT population. Times to engraftment were compared, with competing risk events treated as censored observations. Note that a hazard ratio >1 indicates benefit to the omidubicel arm, since engraftment is a beneficial event. The hazard ratio for engraftment in the omidubicel arm compared to the unmanipulated

CBU arm was 2.25 (95% CI 1.42-4.25, p<0.001), supporting the primary endpoint analysis (Table 14.2.1.5.1) (Figure 3).

Figure 3: Kaplan-Meier Curve for Neutrophil Engraftment (ITT Population)

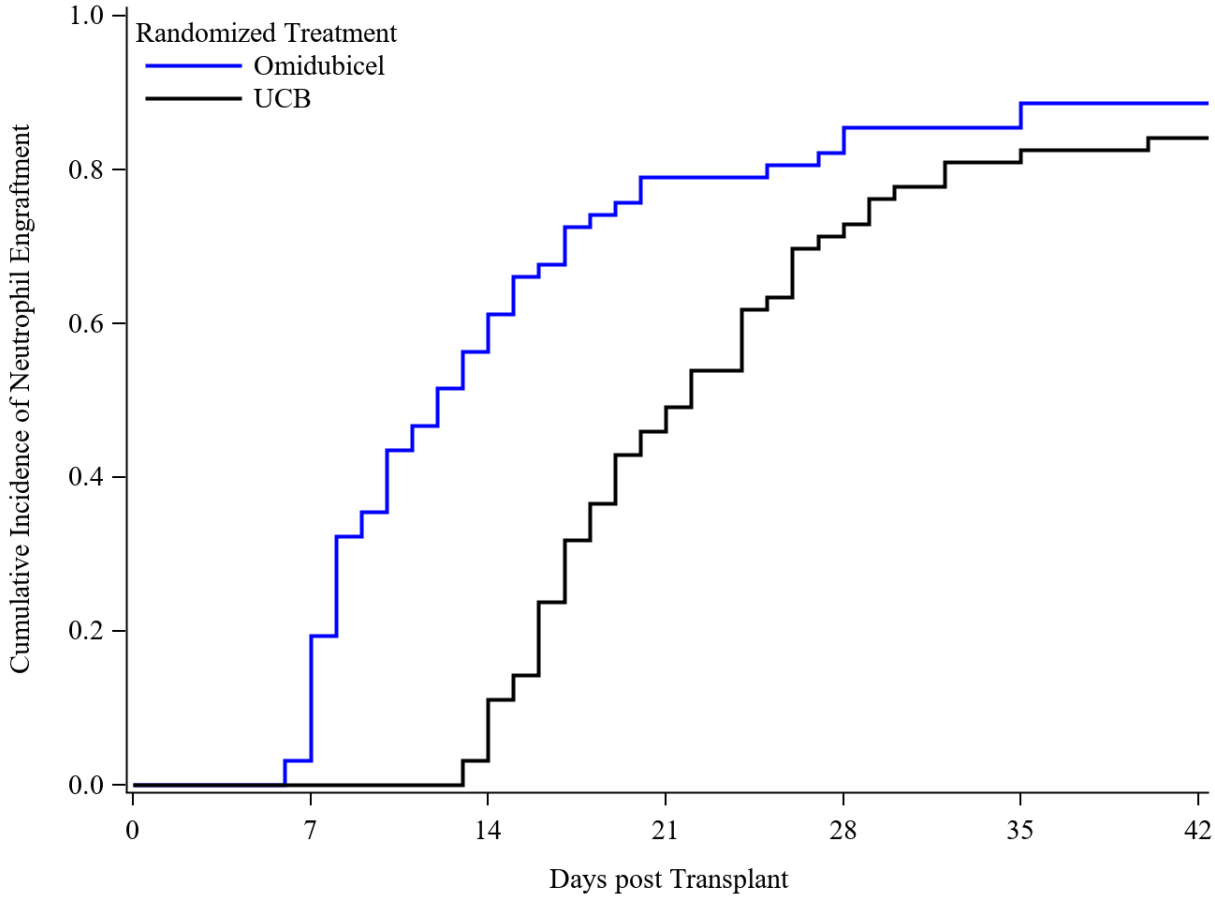


N at risk							
Omidubicel	62	57	24	10	8	6	2
UCB	63	59	57	30	13	7	4

Data Source: Listing 16.2.6.12

Note: UCB= Unmanipulated cord blood unit arm

Figure 4: Cumulative Incidence of Neutrophil Engraftment (ITT Population)



Data Source: Listing 16.2.6.12

Note: UCB= Unmanipulated cord blood unit arm

An additional analysis was performed in patients in the AT population who received a transplant that met protocol specifications and were grouped according to the treatment actually received. Similar to the results in the ITT population, with a median time to engraftment of 10 days (95% CI 8-13) for the omidubicel group, and 20 days (95% CI 18-24) for the unmanipulated CBU group, the time to neutrophil engraftment in the AT population was shortened by omidubicel transplantation compared to umbilical CBT (p<0.001) (Table 14.2.1.3.1, Table 14.2.1.3.2).

A similar analysis was also performed in the AEP population, focused on the patients who achieved neutrophil engraftment by 42 days post-transplant, further confirming the shorter time to neutrophil engraftment in the omidubicel group (10 days (95% CI 8-12) for the omidubicel group versus 19 days (95% CI 17-22) for the unmanipulated CBU group, p<0.001) (Table 14.2.1.4.3).

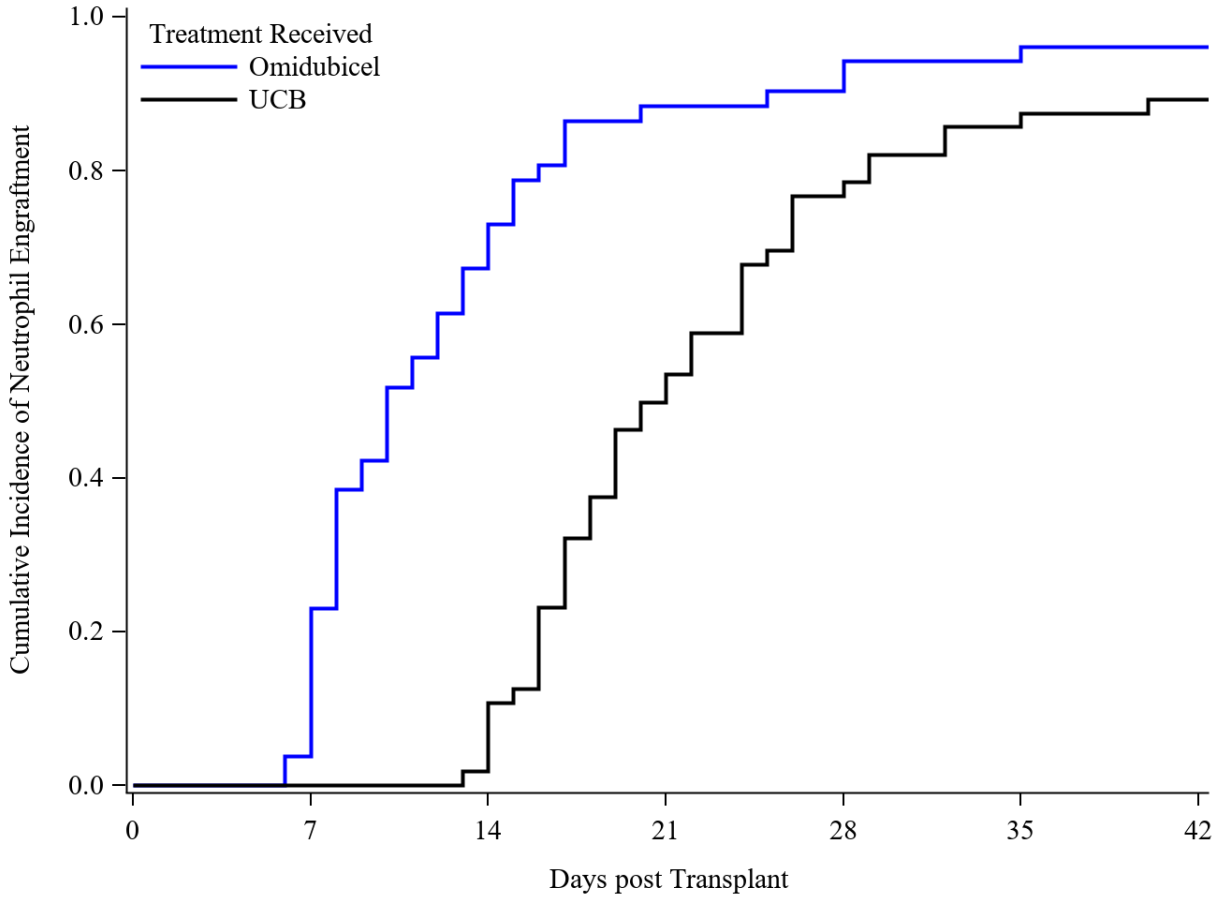
11.4.1.2 Neutrophil Engraftment by 16 Days and 42 Days Following Transplantation

In order to allow for a direct clinical assessment of engraftment in the patients as-treated, neutrophil engraftment was assessed in the AT population. As shown in Figure 5, 96% of

patients who received omidubicel (AT population) achieved successful neutrophil engraftment by 42 days post-transplant, compared to 89% of patients who received unmanipulated CBU.

The cutoff on Day 16 was selected to represent the median time of neutrophil engraftment following peripheral blood donor transplantation, considered to be the most rapid hematopoietic recovery following myeloablative HSCT(Bishop, Tarantolo et al. 2000). For the AT population, 81% of omidubicel patients achieved neutrophil engraftment by Day 16 compared to 23% in the unmanipulated CBU group, demonstrating a significantly higher engraftment rate by Day 16 for the omidubicel group ($p<0.001$) (Table 14.2.7.3). The difference in engraftment by Day 16 was also statistically significant ($p<0.001$) in the ITT comparison as well as in the TP ($p<0.001$) (Table 14.2.7.1, Table 14.2.7.2).

Figure 5: Cumulative Incidence of Neutrophil Engraftment (AT Population)



Data Source: Listing 16.2.6.12

Note: UCB= Unmanipulated cord blood unit treatment group

Descriptive subgroup analysis was performed for the following subgroups; disease risk group, age group, intention to perform single versus double CB transplant, disease, HCT-specific Comorbidity Index, gender, race/ethnicity, and geographical region. P-values were not calculated for any of the comparisons due to the small sample sizes and multiple comparisons. Results of these descriptive statistics provided in Table 14.2.1.8.1, Table 14.2.1.8.2, Figure 14.2.1.8.1, and Figure 14.2.1.8.2 demonstrate that the results in the primary endpoint analyses were shown to be

consistent across subgroups. The median day for neutrophil engraftment was shorter for omidubicel across all subgroups.

In summary, the study met its primary endpoint, demonstrating that patients randomized to receive omidubicel engrafted neutrophils 10 days earlier than patients randomized to receive unmanipulated CBU. This result is robustly consistent across the different analysis populations and supports the benefit of the expansion of CBU-derived stem and progenitor cells to meaningfully decrease the duration of post-transplant neutropenia and allow the recovery from the transplant procedure to begin earlier.

11.4.2 Platelet Engraftment

This section includes the efficacy results of two endpoints that assessed platelet engraftment:

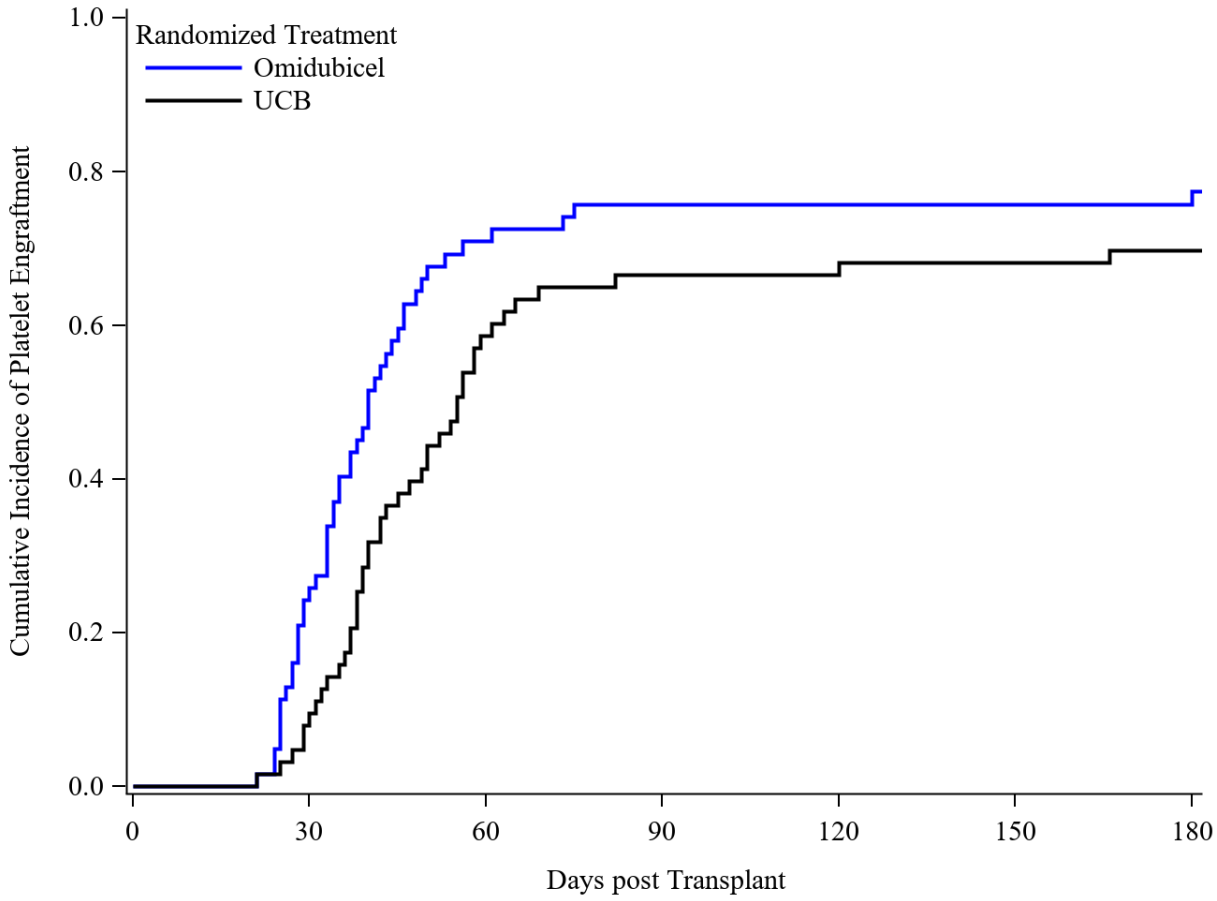
1. Secondary endpoint: Platelet engraftment by 42 days following transplantation
2. Exploratory endpoint: Time from transplantation to platelet engraftment

11.4.2.1 Platelet Engraftment by 42 Days

Table 14.2.4.1.1 presents the events around platelet engraftment for the ITT population.

Platelet engraftment was defined as the first day of three consecutive measurements on different days with platelet count > 20 $\times 10^9$/L in the absence of platelet transfusions in the preceding seven days. Table 14.2.4.1.2 and Figure 6 show the cumulative incidence of patients with platelet engraftment and the time to platelet engraftment through Day 42 in the ITT population. The percentage of patients achieving platelet engraftment by Day 42 was 55% (n=34) in those randomized to receive omidubicel compared to 35% (n=22) in those randomized to receive unmanipulated CBU. The absolute difference in incidence was 20% (rerandomization 95% CI 3% – 35%; p=0.028) (Table 14.2.4.1.2). After adjusting the p-value for multiple comparisons using Hommel's test, the p-value remained as 0.028 (see Section 11.4.8.4, Table 21).

Figure 6: Cumulative Incidence of Platelet Engraftment by 180 Days following Transplantation (ITT Population)



Data Source: Listing 16.2.6.7

Note: UCB= Unmanipulated cord blood unit arm

The higher proportion of omidubicel patients engrafting platelets by Day 42 time was also demonstrated in a secondary analysis where pre-transplant relapse was considered a competing risk (p=0.042) (Table 14.2.4.4.1).

The secondary analysis in the AT population provided similar results confirming the results are consistent when looking at only patients who received the actual treatment. Table 14.2.4.3.1 shows the proportion of patients with platelet engraftment by Day 42 post-transplant in the AT population. An estimated 63% of the patients treated with omidubicel achieved platelet engraftment within 42 days following transplant, compared to 39% of the patients treated with unmanipulated CBU. The absolute difference of 24% (95% CI 6% – 43%) demonstrates a benefit for treatment with omidubicel (p = 0.011) (Table 14.2.4.3.1). A secondary analysis in the TP population showed a similar absolute difference (21%) benefiting omidubicel (p=0.019) (Table 14.2.4.2.1).

Descriptive subgroup analyses were performed for the following subgroups; disease risk group, age group, intention to perform single versus double CB transplant, disease, HCT-specific

Comorbidity Index, gender, race/ethnicity, and geographical region. P-values were not calculated for any of the comparisons due to the small sample sizes and multiple comparisons. Results are provided in Table 14.2.4.5.1, Table 14.2.4.5.2, Figure 14.2.4.5.1, and Figure 14.2.4.5.2. Inspection of these descriptive statistics generally demonstrated a consistently higher incidence of platelet engraftment by 42 days post-transplant.

The study demonstrated a consistent advantage for omidubicel transplantation in early platelet engraftment. This outcome is in line with the rapid neutrophil engraftment observed with omidubicel, as neutrophil recovery heralds the recovery of the other hematopoietic lineages.

11.4.2.2 Time to Platelet Engraftment

The time to platelet engraftment was analyzed among the patients who achieved platelet engraftment by 180 days post-transplant. Forty-four patients treated with omidubicel and 42 patients treated with unmanipulated CBU engrafted platelets by 180 days.

For the PEP population, omidubicel patients engrafted on average 8 days faster than unmanipulated CBU patients. Among the patients achieving engraftment, the median time to platelet engraftment in patients treated with omidubicel was 34 days (range, 21-180 days), compared to 42 days (range, 21-120 days) in patients treated with unmanipulated CBU. The Cox regression hazard ratio was 1.54 (95%CI 1.02-2.63, p=0.050) (Table 14.2.8.1.1).

A secondary analysis on the ITT population demonstrated a median time to engraftment of 40 days for the omidubicel arm, compared to 55 for unmanipulated CBU arm. The hazard ratio for faster engraftment on the omidubicel arm was 1.49 (95%CI 0.97-2.33, p=0.058) (Table 14.2.8.2.1).

A post hoc analysis of platelet engraftment was performed on the AT population. The cumulative incidence of platelet engraftment by Day 100 following transplantation was 83% at a median of 37 days (95% CI 33-42 days) compared to 73% at median of 50 days (95% CI 42-58 days) for the controls (p=0.023) (Table 14.2.8.3.1).

These differences further confirm the advantage of treating patients with omidubicel in platelet engraftment post-transplant.

11.4.3 Infections

This section includes the efficacy results of three endpoints that assessed infections:

1. Secondary endpoint: Incidence of Grade 2/3 bacterial or invasive fungal infections by 100 Days following transplantation
2. Exploratory endpoints: Grade 3 viral infections by 180 days and one year following transplantation

11.4.3.1 Bacterial and Fungal Infections

Patients randomized to omidubicel had a lower incidence of Grade 2/3 (moderate – severe) bacterial or invasive fungal infections by 100 Days following transplantation compared to patients randomized to control. Table 18 and Figure 7 present the cumulative incidence of patients with a first Grade 2/3 bacterial infection or invasive fungal infection between randomization and 100 Days following transplantation, in the ITT population. Thirty-nine percent of the patients randomized to receive omidubicel had a Grade 2-3 bacterial infection or

invasive fungal infection within 100 Days following transplant, compared to 60% of the patients randomized to receive unmanipulated CBU, demonstrating an absolute difference of 22% (95% CI 3% – 38%; p=0.016). After adjusting the p-value for multiple comparisons using Hommel's test, the p-value was 0.028 (see Section 11.4.8.4, Table 21). This difference in cumulative incidence in favor of omidubicel was also seen in a post hoc analysis at Day 180 (25% difference, 95% CI 7%-41%) and Day 365 (25% difference, 95% CI 9% - 41%; re-randomization p-value = 0.007) (Table 14.2.2.2.1, Table 14.2.2.2.2, Figure 14.2.2.2.1).

Interestingly, nearly 50% of patients randomized to unmanipulated CBU experienced a first infection within the first 10 days post-transplant (Figure 7). This observation highlights the increased susceptibility of patients to serious infections during the period of peri-transplant neutropenia. The cumulative incidence curves begin to separate at approximately 7 days post-transplant, mirroring the timelines for neutrophil engraftment (Figure 5). These apparent kinetics further support the biological link between neutrophil recovery and infections and emphasize the importance of rapid neutrophil recovery post-transplant.

Table 18: Incidence of First Bacterial Infection Grades 2-3 or Invasive Fungal Infection by 100 Days following Transplantation (ITT Population)

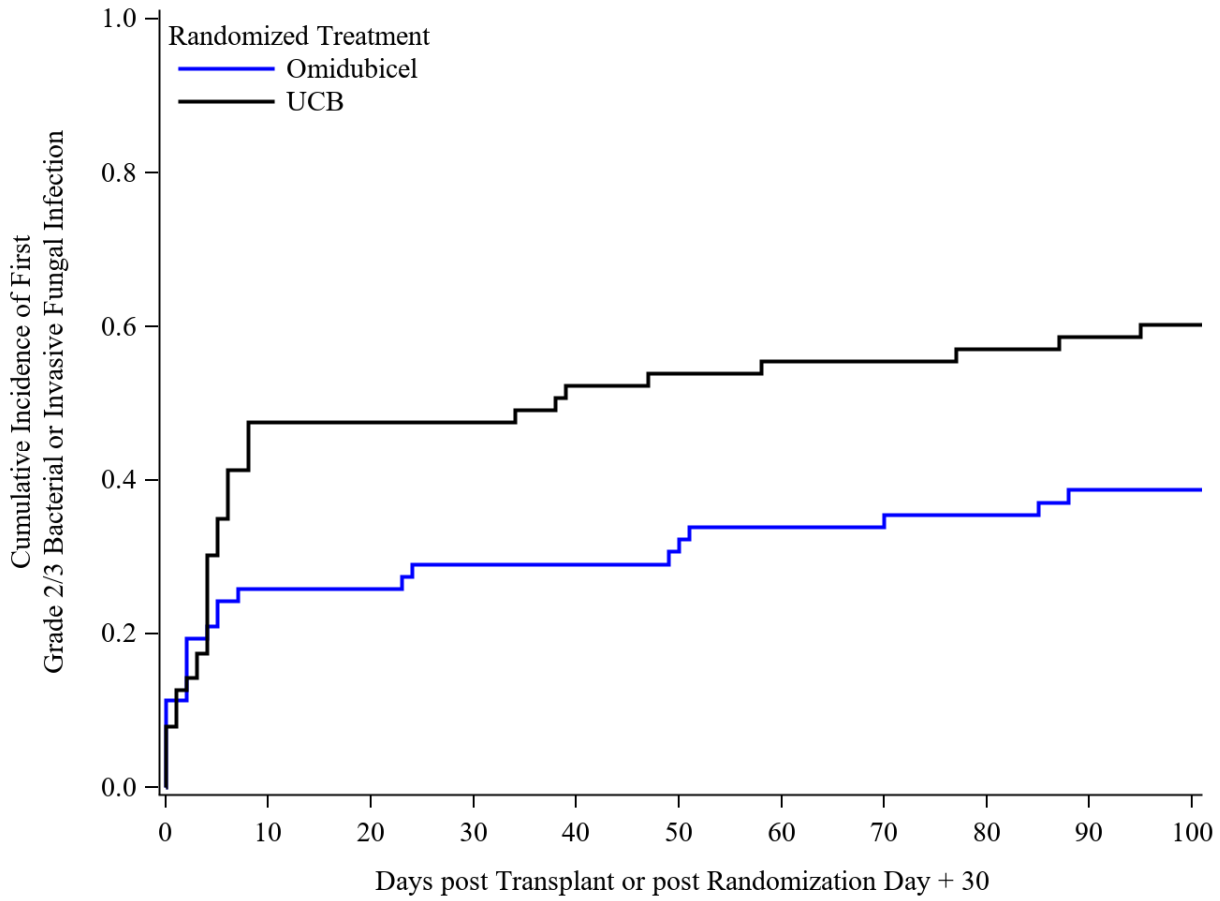
	Patients				Cumulative Incidence			Test for Difference in Cumulative Incidence
Randomized Treatment Group	At Least One Event[a] (N)	Only Bacterial Infections (N)	Only Fungal Infections (N)	Bacterial and Fungal Infections (N)	Day 100 Cumulative Incidence	Difference in Cumulative Incidence (Omidubicel vs UCBU)	Rerandomization Confidence Intervals for Difference in Cumulative Incidence	Re-randomization *P*-Value
Omidubicel	24	20	2	2	0.39	-0.22	95% CI: -0.38, -0.03	0.016
UCBU	38	30	0	8	0.60			

Data Source: Listing 16.2.6.5

[a] This table includes all post-randomization infections through Day 100 post-transplant for those transplanted or through Day 130 post-randomization for those not transplanted.

Abbreviations: CI: Confidence interval; UCBU: Unmanipulated cord blood unit

Figure 7: Cumulative Incidence of First Bacterial Infection Grades 2-3 or Invasive Fungal Infection by 100 Days following Transplantation (ITT Population)



Data Source: Listing 16.2.6.5

Note: Days are calculated from Randomization Day +30 for those who do not receive a transplant by Day 90 post randomization; UCB= Unmanipulated cord blood unit arm

The statistically significant difference in infection incidence was also demonstrated in the AT population. A Grade 2-3 bacterial infection or invasive fungal infection within 100 Days following transplant occurred in 35% of patients treated with omidubicel, compared to 61% of patients treated with unmanipulated CBU, demonstrating an absolute difference of 26% (95% CI 8% – 44%; p=0.006) (Table 14.2.2.1.3). A similar reduced incidence of infection (23%) was seen in a secondary analysis of the TP population (p=0.011) (Table 14.2.2.1.2).

Descriptive subgroup analyses were performed for the following subgroups; disease risk group, age group, intention to perform single versus double CB transplant, disease, HCT-specific Comorbidity Index, gender, race/ethnicity, and geographical region. P-values were not calculated for any of the comparisons due to the small sample sizes and multiple comparisons. Results are provided in Table 14.2.2.1.5 and Figure 14.2.2.1.2. Inspection of these descriptive statistics demonstrates a consistently lower incidence of infections across the subgroups.

Infection prophylaxis procedures can vary between study sites as well as between individual patients at a site depending on patient characteristics and ensuing circumstances. Review of

infection prophylaxis data did not reveal any differences that might affect the incidence of infection between treatment groups in this study (Table 14.3.9.4 and Table 14.3.9.5). The use of infection prophylaxis was similar between the two treatment groups. In the AT population, 100% of patients on the omidubicel arm reported using at least one anti-bacterial prophylaxis compared to 93% on the unmanipulated CBU arm. The most common anti-bacterial agents were ciprofloxacin (48% of omidubicel patients and 45% of unmanipulated CBU patients) and levofloxacin (46% of omidubicel patients and 54% of unmanipulated CBU patients). Anti-fungal prophylaxis was used in 94% of omidubicel patients and 96% of unmanipulated CBU patients. The most common anti-fungal agents for omidubicel and unmanipulated CBU patients were posaconazole (67% vs 66%), fluconazole (33% vs 32%), micafungin (31% vs 23%), and voriconazole (29% vs 25%). All patients in the AT population received anti-viral prophylaxis with the majority receiving acyclovir (88% of omidubicel patients and 89% of unmanipulated CBU patients).

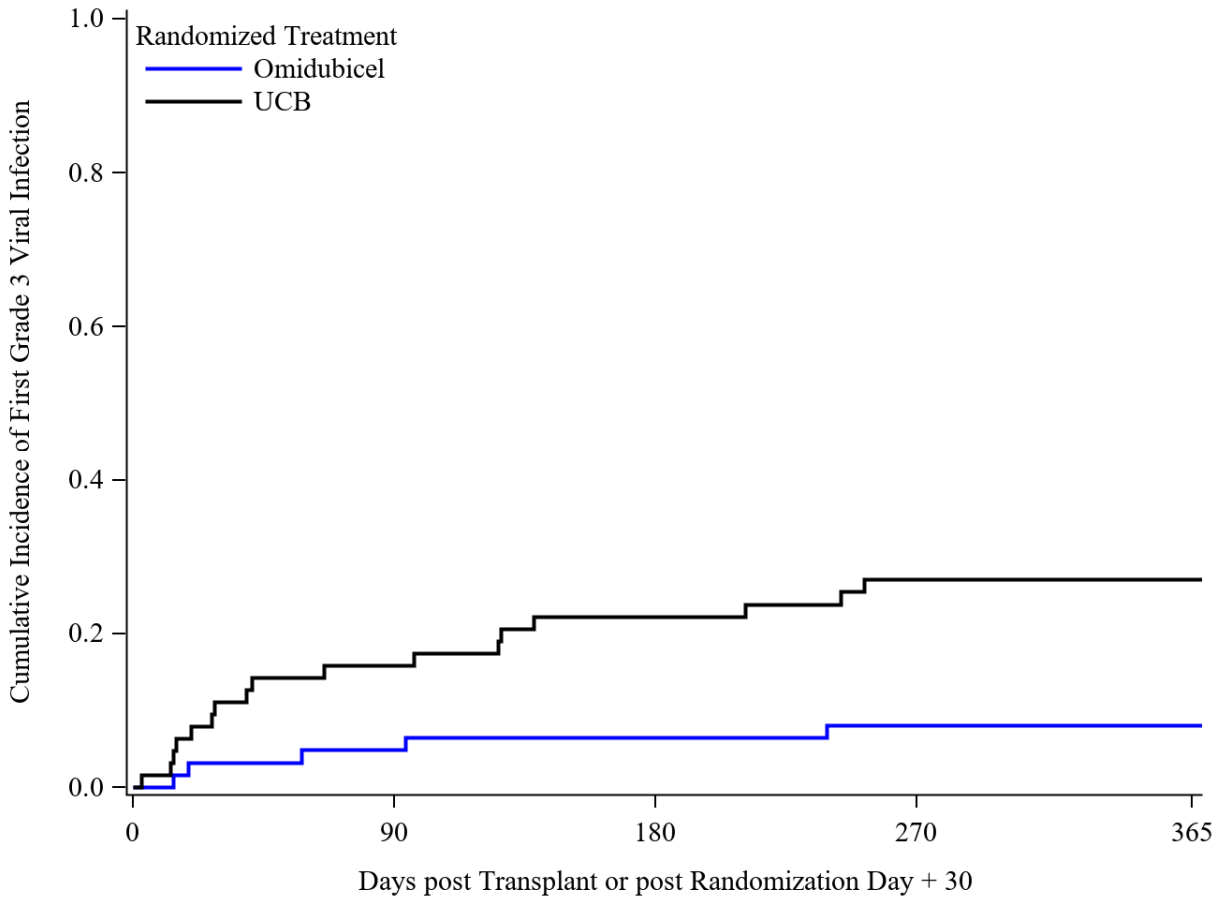
11.4.3.2 Viral Infections

The cumulative incidence of Grade 3 (severe) viral infections in the year post-transplant was analyzed as an exploratory endpoint to further assess the impact of omidubicel on infectious complications following transplantation.

Omidubicel patients were less likely than unmanipulated CBU patients to experience a Grade 3 viral infection. In the ITT population, 8% of patients randomized to omidubicel had a Grade 3 viral infection within 1-year following transplant compared to 27% of patients randomized to unmanipulated CBU, demonstrating an absolute difference of 19% (95% CI 6% – 33%; p=0.004, Figure 8) (Table 14.2.22.1.1, Figure 14.2.22.1.1).

In the AT population, the cumulative incidence of Grade 3 viral infections at one year was also 8% in the omidubicel group compared to 27% in the unmanipulated CBU group, representing a difference in cumulative incidence of 19% (95% CI 6-33, p=0.007) favoring the omidubicel group (Table 14.2.22.3.1, Figure 14.2.22.3.1). Differences in cumulative incidence for the TP population were also statistically significant in favor of the omidubicel arm (8% vs 29%; p=0.003) (Table 14.2 22.2.1, Figure 14.2.22.2.1).

Figure 8: Cumulative Incidence of First Grade 3 Viral Infection by 1 Year Following Transplantation (ITT Population)



Data Source: Listing 16.2.7.10

Note: UCB= Unmanipulated cord blood unit arm

Analyses of Grade 3 viral infections by 180 days following transplant also showed a lower incidence of infections in the omidubicel group compared to unmanipulated CBU, in the ITT population (6% vs. 22%; p=0.016), TP population (7% vs. 24%; p=0.008), and in the AT population (6% vs. 21%; p=0.015).

Additional details on overall infection experience and infection density are provided in Section 12.2.3.10 (Table 14.2.21.1.1, Table 14.2.21.2.1, Table 14.2.21.3.1).

One of the most meaningful impacts of the delayed hematopoietic recovery with standard CBU transplantation, is the increased risk of infections. Bacterial and fungal infections are particularly associated with the extent of neutropenia following transplantation, and the risk of all infections is dependent on a rapid and complete recovery of the hematopoietic and immune functions following transplantation. Patients randomized to receive omidubicel demonstrated a lower risk of developing bacterial or fungal infections in the early period following transplantation, compared to patients randomized to unmanipulated CBU. The risk of developing viral infections was lower throughout the entire year following transplantation, which may suggest a robust recovery of antimicrobial functional mechanisms following transplantation.

These results are consistent with the primary study outcome, and robustly support the clinical efficacy of omidubicel.

11.4.4 Hospitalization (Days Alive and Out of Hospital, Duration of Primary Hospitalization),

This section includes the efficacy results of two endpoints that assessed hospitalization:

1. Secondary endpoint: Days alive and out of hospital (OOH) in the first 100 Days following transplantation
2. Exploratory endpoint: Duration of primary hospitalization

11.4.4.1 Days Alive and Out of Hospital

Days alive and OOH was calculated by subtracting the total number of days in the hospital during the first 100 Days post-transplant from 100 (for patients alive at 100 Days) or from the day of death (for patients who died in the first 100 days). Patients who were not transplanted by Day 90 post-randomization were assigned a value of zero for total days alive and OOH. Table 19 and Table 20 present information on the number of days alive and OOH in the first 100 Days following transplant in the ITT population. Table 19 shows that in both the omidubicel and unmanipulated CBU groups, the majority of patients received a transplant and were followed for at least 100 days. Table 20 shows that those randomized to receive omidubicel had more days alive and OOH (median = 60.5) than patients randomized to receive unmanipulated CBU (median = 48.0; Mann-Whitney test of difference, p=0.005). After adjusting the p-value for multiple comparisons using Hommel's test, the p-value was 0.014 (Section 11.4.8.4, Table 24). The probability that a patient on omidubicel had more days alive and OOH than a patient receiving unmanipulated CBU was 63% (95% CI 54% – 72%). This analysis demonstrated that transplantation with omidubicel rather than unmanipulated CBU was associated with increased time alive and OOH in the first 100 Days following transplant.

Table 19: Status for Days Alive and Out of Hospital in the First 100 Days following Transplantation (ITT Population)

	Transplanted by Day 90 post Randomization		
Randomized Treatment Group	**Not Transplanted by Day 90 post Randomization[a] (n)**	**100 Days of Follow-up Post-transplant (n)**	**Died within First 100 Days (n)**
Omidubicel	3	53	6
UCBU	4	49	10

Data Source: Listing 16.2.6.6

[a] For this group, days alive and out of hospital are assigned as 0.

Abbreviations: UCBU: Unmanipulated cord blood unit

Table 20: Statistical Test of Days Alive and Out of Hospital in the First 100 Days following Transplantation (ITT Population)

Randomized Treatment Group	N	Min	Lower Quartile	Median	Upper Quartile	Max	Probability of More Days Alive and out of Hospital	Re-randomization 95% Confidence Interval		Re-randomization *P*-Value
Omidubicel	62	0.0	33.0	60.5	76.0	89.0	0.63	0.54	0.72	0.005
UCBU	63	0.0	6.0	48.0	67.0	84.0				

Data Source: Listing 16.2.6.6
Abbreviations: UCBU: Unmanipulated cord blood unit

The secondary analysis in the AT population provided similar results to the ITT analysis, confirming the results are consistent when looking at only patients who received the actual treatment. Those treated with omidubicel had a median of 62.5 days alive and OOH, compared to 50.5 days for patients treated with unmanipulated CBU (p=0.01). (Table 14.2.3.3.2). Results were nearly identical when repeated in the TP population (Table 14.2.3.2.2).

Descriptive subgroup analyses were performed for the following subgroups; disease risk group, age group, intention to perform single versus double CB transplant, disease, HCT-specific Comorbidity Index, gender, race/ethnicity, and geographical region. P-values were not calculated for any of the comparisons due to the small sample sizes and multiple comparisons. Results are provided in Table 14.2.3.4.1, Table 14.2.3.4.2 and Figure 14.2.3.4.1. Inspection of these descriptive statistics generally demonstrated a consistently higher number of days alive and OOH for the omidubicel group. Lymphoma patients (n=5) had a lower number of days alive and OOH in the omidubicel group. Given the small number of lymphoma patients, this result is likely a random finding.

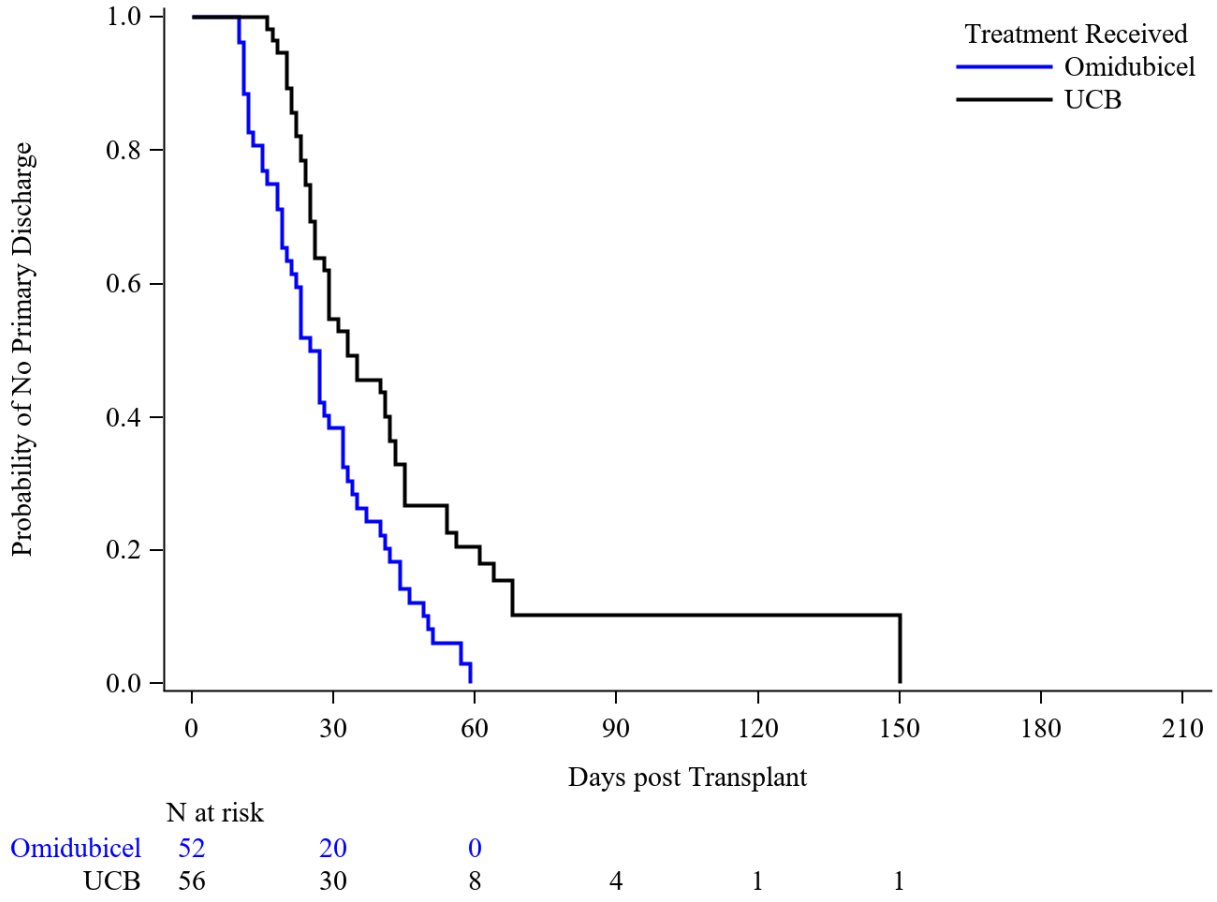
When assessing the days alive and OOH within the first 100 days post-transplant in the AT population, the following were noted: among US centers the days OOH were 8.5 days higher for omidubicel recipients (67 days vs. 58.5 days), while among EU centers this difference was five days (54 vs. 49 days) in favor of omidubicel. This difference may be reflective of different hospitalization practices in different geographies. Among other countries (Singapore, Brazil, Israel) the difference in days OOH was 39 days (39 days for omidubicel recipients vs. 0 days), possibly impacted by a number of inexperienced centers in these geographies. This observation is possibly supported by the difference between high enrolling centers (six patients or more enrolled on the study) compared to lower enrolling centers (five patients or less). Among high enrolling centers, reflecting also a higher level of experience, the difference in the days OOH was 12.5 days in favor of omidubicel (71 days vs. 58.5 days). In low enrolling centers, this difference was 20.5 days in favor of omidubicel (55 vs. 34.5 days). Interestingly, the differences in the days OOH for the two primary disease diagnoses, AML and ALL, was 23 days (62 vs. 39 days in favor of omidubicel) in AML patients and 19.5 days (67.5 vs. 48.0 days also in favor of omidubicel) in ALL patients. As noted above, the differences observed were generally consistent with the overall study outcomes, however the interpretation was limited by the small sample size.

11.4.4.2 Duration of Primary Hospitalization

None of the patients in this study were transplanted as outpatients. Compared to patients in the unmanipulated CBU arm, patients in the omidubicel arm spent less time in the hospital during their primary hospitalization for transplant. In the TP population, the median duration of the primary hospitalization was 27 days in the patients transplanted on the omidubicel arm, compared to 35 days in the patients transplanted on the unmanipulated CBU arm (hazard ratio (HR)=1.7; 95% CI: 1.2, 2.7; p=0.005) (Table 14.2.9.1.1).

The primary hospitalization difference between treatment arms in the AT population was also statistically significant. In order to provide a direct comparison of patients as they were treated, the Kaplan-Meier curve of time from transplant to discharge in the AT population is presented in Figure 9.

Figure 9: Time to Discharge for Primary Hospitalization for Transplant (AT Population)



Data Source: Listing 16.2.6.16

Note: UCB= Unmanipulated cord blood unit treatment group

In the AT population, the median time from transplant to discharge was 25 days for the omidubicel arm compared to 33 days for the unmanipulated CBU arm (HR=2.0, 95%CI 1.4-3.0, p<0.001) (Table 14.2.9.2.1).

Differences in the initial hospital stay are reflective of the differences between treatment groups in times to engraftment and the incidence of infections during the early post-transplant period. However, the difference in days alive and OOH (median 12-day difference in AT population) does not appear to be entirely explained by differences in the initial transplant hospitalization (median 8 days difference in AT population) suggesting an additional benefit of omidubicel beyond the initial peri-transplant neutropenia.

The demonstrated rapid hematopoietic recovery with omidubicel, spanning both neutrophil and platelet engraftment, is consistent with the decreased occurrence of infections, and the impact on the primary and subsequent hospital admissions. The hospitalization duration of patients treated with unmanipulated CBU demonstrate a clinically meaningful advantage for omidubicel in improving the time alive and OOH by 10-15 days.

11.4.5 Relapse & Survival

This section includes the results of the following endpoints that assessed relapse and survival:

1. NRM: Assessed as a tertiary endpoint at 210 day following randomization and as an exploratory endpoint at both 130 days and 15 months following randomization
2. Overall survival: Assessed as an exploratory endpoint at 210 days and 15 months following randomization.
3. Disease-free survival: Assessed as an exploratory endpoint at 15 months following randomization
4. Relapse and relapse mortality: Assessed as exploratory endpoints at 15 months and one year following randomization

11.4.5.1 Non-Relapse Mortality

Non-relapse mortality is often referred to as transplant-related mortality (TRM) and defined as death not preceded by relapse as detected by protocol-mandated monitoring of disease recurrence post-transplant.

Non-relapse mortality was analyzed at 130 days, 210 days and 15 months following randomization, with secondary analysis at 100 days, 180 days and 1 year following transplantation in the ITT population (Table 21). In these secondary analyses, the origin of the time axis was the day of transplant which allowed for a more direct comparison of the mortality risks associated with transplantation. Non-relapse mortality that occurred between randomization and transplant was counted as an event at Time 0.

Table 21: Non-Relapse Mortality (ITT Population, %)

Timepoint	Omidubicel	UCBU	Difference; 95%CI; *P*-Value[a]
130 Days Post Randomization	6	14	8; 95% CI: -3, 19; p=0.25
100 Days Post-Transplantation	10	13	3; 95% CI: -8, 14; p=0.78
210 Days Post Randomization	11	24	13; 95% CI: -2, 25; p=0.09
180 Days Post-Transplantation	11	22	11; 95% CI: -2, 24; p=0.13
15 Months Post Randomization	15	29	14; 95% CI: 0, 28; p=0.07
One Year Post-Transplantation	15	29	14; 95% CI: 0, 28; p=0.07 Gray's Test: HR=0.48; p=0.06

Data Source: Table 14.2.6.1.1, Table 14.2.6.3.1, Table 14.2.10.1.1, Table 14.2.10.2.1, Table 14.2.11.1.1, Table 14.2.11.2.1

[a] Re-randomization p-value except where otherwise noted

Abbreviations: CI: Confidence interval, HR: Hazard ratio; ITT: Intent-to-treat, NRM: Non-relapse mortality; UCBU: Unmanipulated cord blood unit

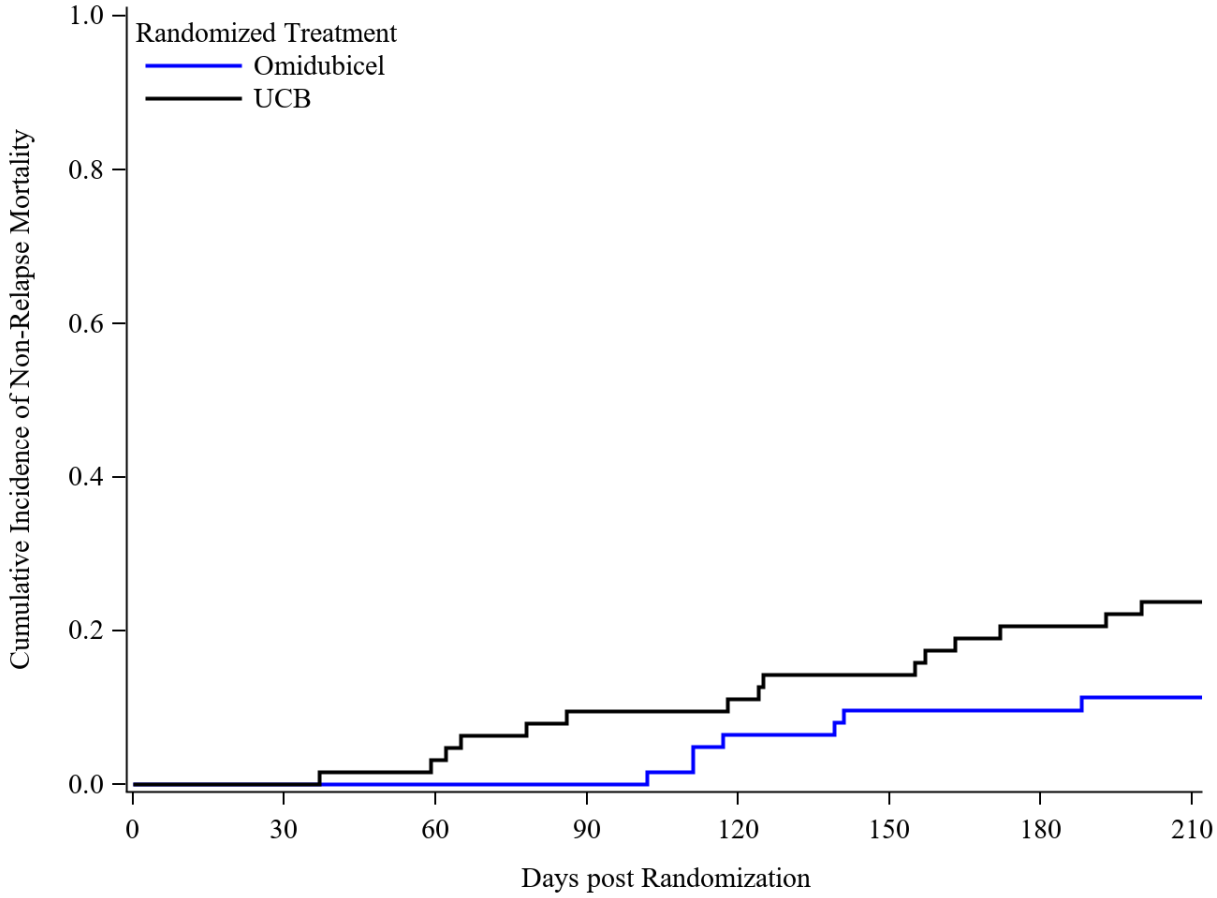
The timepoint of 210 Days post-randomization was selected to coincide approximately with 180 days following transplantation. The cumulative incidence of NRM by 210 Days post- randomization in patients randomized to omidubicel was 11% (7 deaths), compared to 24% (15 deaths) in patients randomized to unmanipulated CBU. Omidubicel demonstrated a non-statistically significant reduction in the 210 Days post-randomization NRM percentage of 13%

with a 95% CI of -2% to 25% (p=0.086, Figure 10). A secondary analysis where relapse prior to transplant was included as a competing risk demonstrated identical results (Table 14.2.6.2.1).

A secondary analysis in the ITT population assessed NRM by 180 days post-transplant. In this analysis, NRM that occurred between randomization and transplant was counted as an event at Time 0. The results were similar to those of the primary analysis, demonstrating 11% NRM for omidubicel compared to 22% for unmanipulated CBU (p=0.13) (Table 14.2.6.3.1).

At 15 Months after randomization, the reduction in cumulative incidence of NRM for the omidubicel arm was 14% (from 29% to 15%) with a 95% CI of 0% to 28% (p=0.068) (Table 14.2.11.1.1).

Figure 10: Cumulative Incidence of NRM by 210 Days following Randomization (ITT Population)



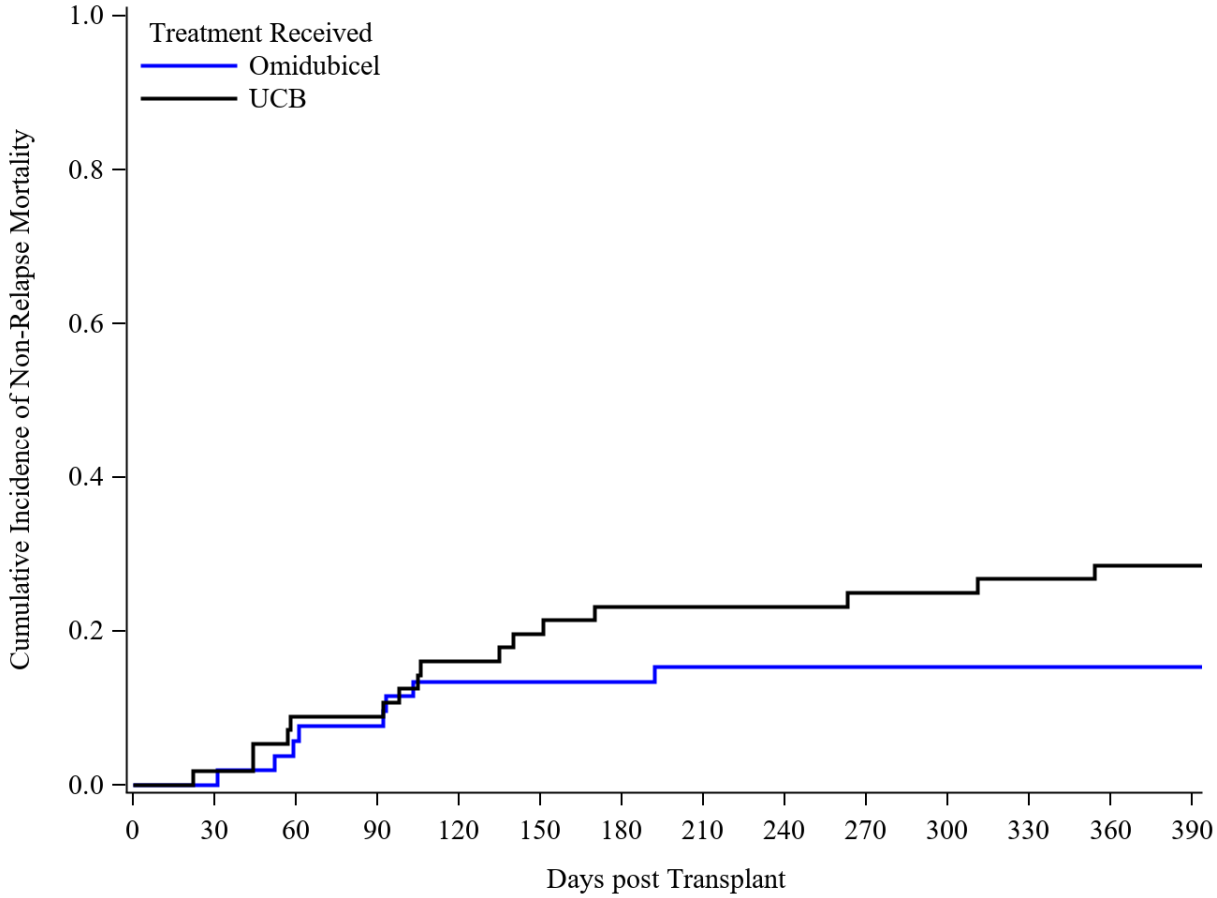
Data Source: Listing 16.2.6.2

Note: UCB= Unmanipulated cord blood unit arm

NRM is perhaps more easily understood in the AT population as pre-transplant events and events in patients not transplanted would not generally be considered transplant-related. As such, a post hoc analysis of NRM post-transplant in the AT population was performed (Figure 11). By 180 days post-transplant, NRM was 13% for the patients treated with omidubicel, and 23% for patients treated with unmanipulated CBU. At 12 months, the reduction in cumulative incidence

of NRM for the omidubicel arm was 13% (from 29% to 15 %) with a 95% CI of –2% to 29% (Gray's Test p=0.121; Figure 11).

Figure 11: Cumulative Incidence of NRM by One Year following Transplantation (AT Population) [Post Hoc Analysis]



Data Source: Listing 16.2.6.2

Note: UCB= Unmanipulated cord blood unit treatment group

The results described for NRM are in line with the other outcomes for omidubicel. Delayed hematopoietic recovery is associated with a higher risk of post-transplant complications due to the protracted hematopoietic cytopenias, which may result in death. Although the study was not designed to demonstrate a benefit in survival for omidubicel, NRM was numerically lower in the omidubicel arm at 6 months and 1 year following transplantation, in all populations analyzed.

11.4.5.2 Overall Survival

Overall survival estimates at 210 days and 15 months following randomization were generated using the Kaplan-Meier method (Figure 12) and compared between groups in the ITT population (Table 22). A secondary analysis was also performed at 180 days post-transplant.

At 210 days following randomization there was a 16% increase in survival (68%-84%) for omidubicel with a 95% CI of 1% -30% (p=0.04) (Table 14.2.12.1.1, Figure 14.2.12.1.1). The

secondary analysis at Day 180 post-transplant showed a 12% increase in survival (70% to 82%) for omidubicel with a 95% CI of -2%-27% (p=0.11) (Table 14.2.12.2.1, Figure 14.2.12.2.1).

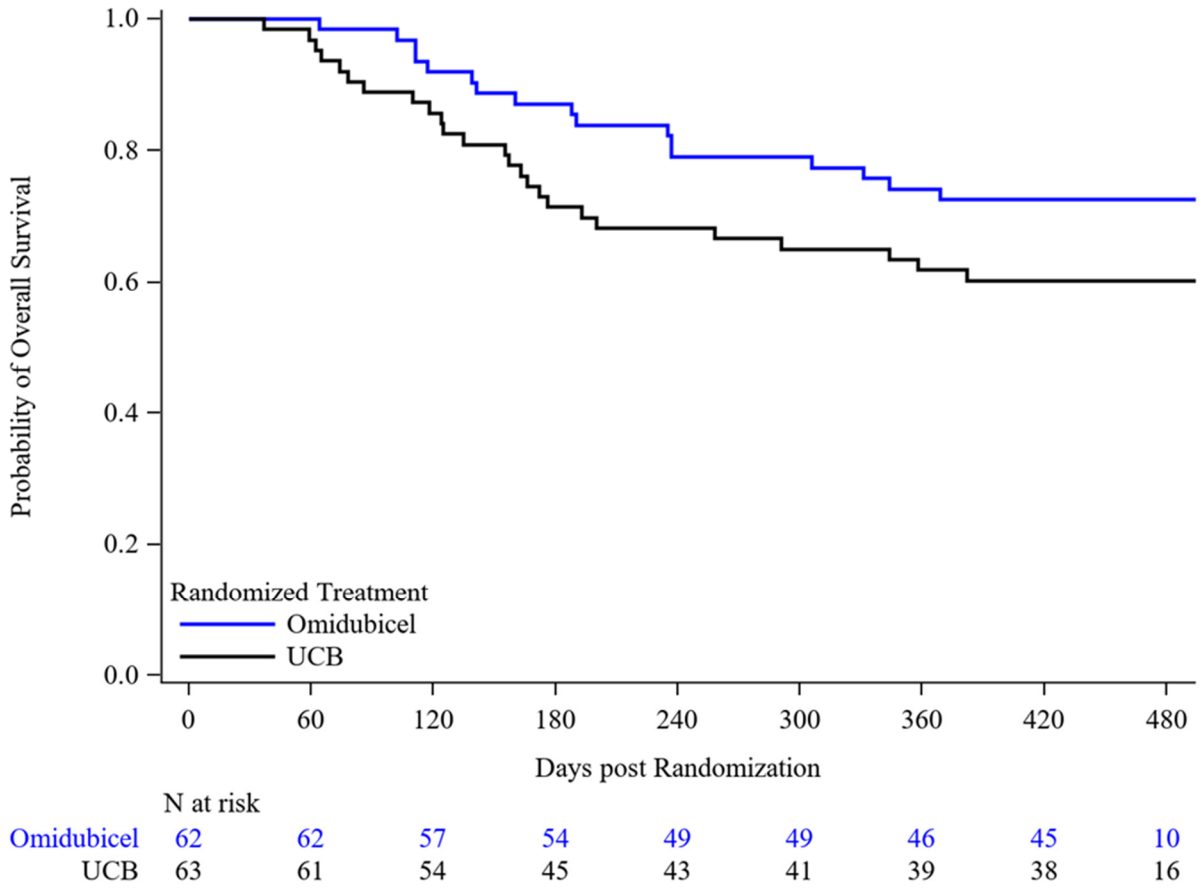
At 15 Months following randomization, there was a 12% increase in survival (60%-73%) for omidubicel with a 95% CI of –5%-28% (p=0.13) (Table 14.2.13.1.1, Figure 14.2.13.1.1).

A post hoc analysis utilized a Cox proportional hazards model with randomized treatment and disease risk as covariates in the model. The adjusted HR for mortality with omidubicel versus unmanipulated CBU was 0.61 (95% CI, 0.32-1.15; p=0.075) (Table 14.2.12.3.1).

A post hoc analysis performed on the AT population also demonstrated a 13% increase in survival (64%-77%) for omidubicel at 1 year post-transplant with a 95% CI of -4%-29% (p=0.14) (Table 14.2.12.3.2, Figure 14.2.12.3.1.

Although the study was not designed to demonstrate a difference in survival, overall survival of omidubicel was significantly higher at 210 Days post-randomization and numerically higher at other timepoints following transplantation.

Figure 12: Overall Survival by 15 Months following Randomization (ITT Population)



Data Source: Listing 16.2.6.2

Note: UCB= Unmanipulated cord blood unit arm

Table 22: Overall Survival and Disease-Free Survival (ITT Population, %)

Endpoint	Timepoint	Omidubicel	UCBU	Difference; 95%CI; P-Value
Overall Survival	210 Days post Randomization	84	68	16; 95% CI: 1, 30; p=0.038
	180 Days post-transplantation	82	70	12; 95% CI: -2, 27; p=0.113
	15 Months post randomization	73	60	12; 95% CI: -5, 28; p=0.134 Cox regression: HR=0.61; 95% CI: 0.32, 1.15; p=0.075
Disease-free Survival	15 Months post randomization	63	56	7; 95% CI: -10, 23; p=0.448 Cox regression: HR=0.76; 95% CI: 0.43, 1.29; p=0.286

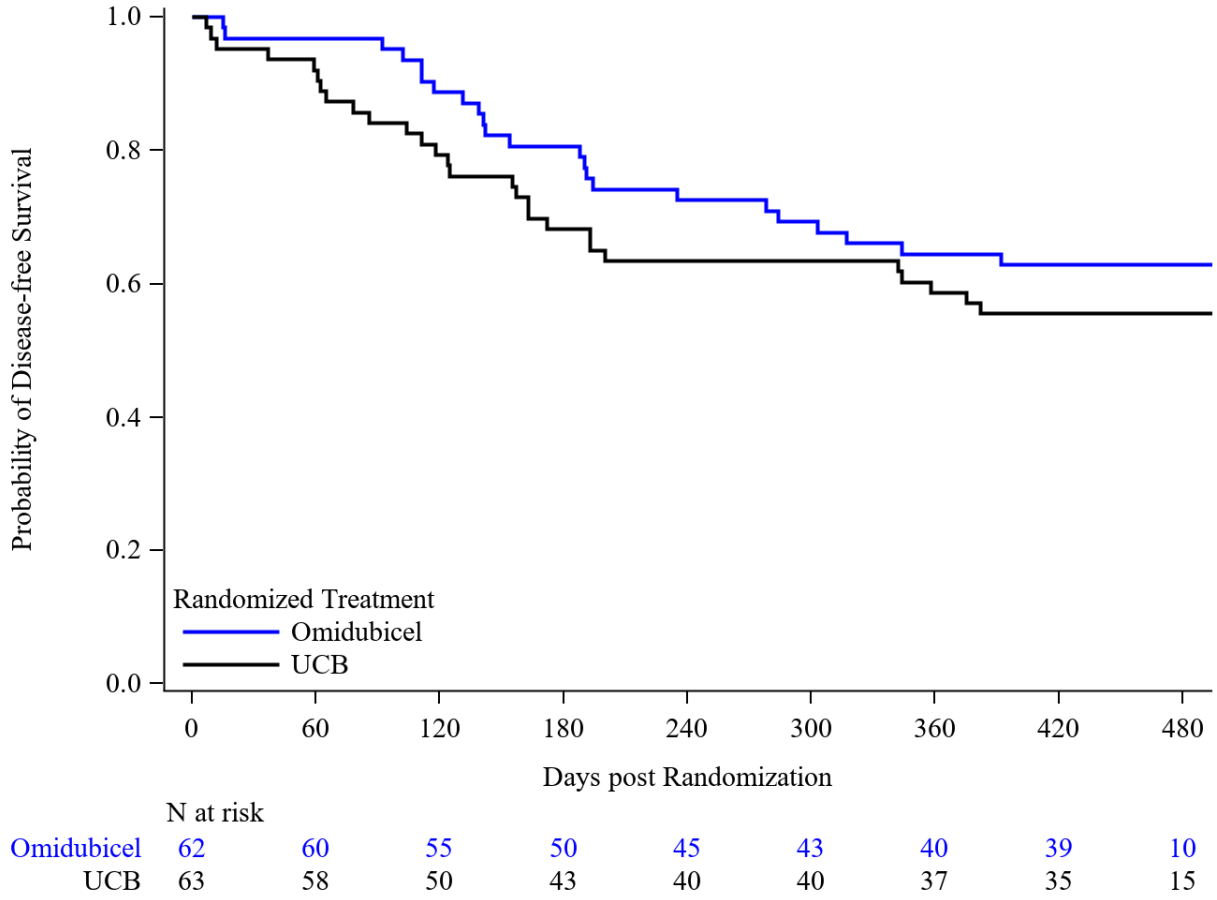
Data Source: Tables 14.2.12.1.1, 14.2.12.2.1, 14.2.12.3.1, 14.2.13.1.1, 14.2.12.3.2, 14.2.13.2.1 and Figures 14.2.12.1.1, 14.2.12.2.1, 14.2.12.3.1, 14.2.13.1.1, 14.2.13.2.1
Abbreviations: CI: Confidence interval; HR: Hazard ratio: UCBU: Unmanipulated cord blood unit.

11.4.5.3 Disease-free Survival

Disease-free survival was evaluated at 15 Months after randomization using the Kaplan-Meier method (Figure 13). Rates of disease-free survival (DFS) were similar between treatment arms. There was a 7% increase in DFS (56% to 63%) for omidubicel with a 95% CI of –10% to 23% (p=0.4, Table 22).

A post hoc analysis utilized a Cox proportional hazards model with randomized treatment and disease risk as covariates in the model. The adjusted HR for treatment failure (relapse or death, inverse of DFS) with omidubicel versus unmanipulated CBU was 0.76 (95% CI, 0.43-1.29; p=0.3) favoring omidubicel (Table 14.2.14.2.1).

Figure 13: Disease-free Survival by 15 Months Following Randomization (ITT Population)



Data Source: Listing 16.2.6.2

Note: UCB= Unmanipulated cord blood unit arm

11.4.5.4 Relapse and Relapse Mortality

Patients underwent protocol-mandated monitoring for relapse at approximate intervals of 3, 6 and 12 Months following transplantation with surveillance appropriate to the underlying disease: morphological, molecular, or cytogenetic evidence of relapse in the setting of leukemia or MDS and new or increased size of lesions on imaging in the setting of lymphoma. The analysis timepoint of 15 Months post-randomization was selected in order to encompass at least one year of post-transplant follow-up.

There were no statistically significant differences in the proportion of patients with relapse between the two treatment arms (Table 23). In the ITT population, Kaplan-Meier probability of relapse was 25% (14 relapses) for patients randomized to omidubicel and 18% (10 relapses) for patients randomized to unmanipulated CBU, reflecting a difference in proportions of 0.07 (95% CI: -0.09 - 0.22, p=0.37). A secondary analysis of the ITT population assessing the cumulative incidence of relapse at the same timepoint demonstrated similar results, with no statistically significant difference in relapse rate between the two study arms (p=0.32), as shown in Figure 14. The cumulative incidence of relapse was 23% for the omidubicel arm and 16% for unmanipulated CBU (Table 14.2.23.1.1).

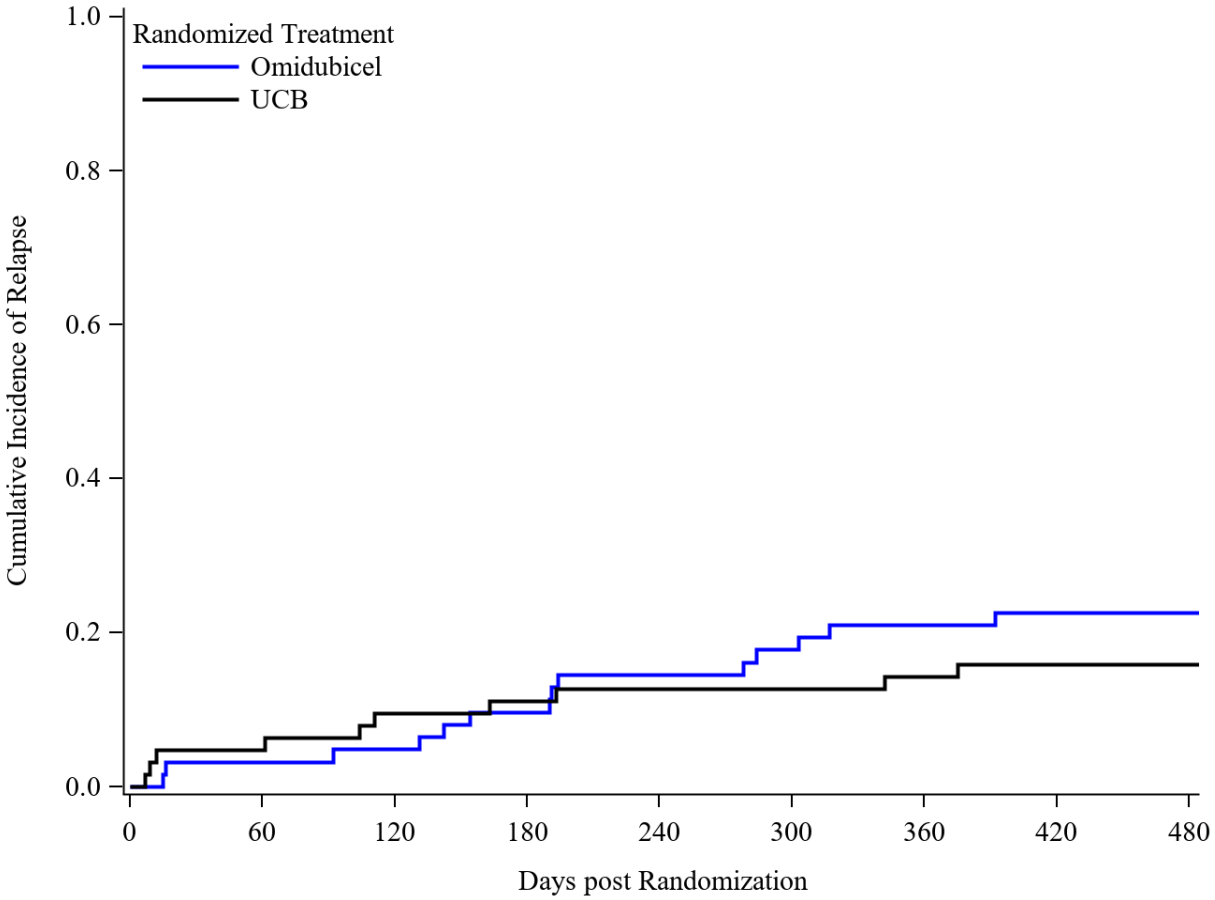
Table 23: Kaplan-Meier Estimate of Relapse by 15 Months following Randomization (ITT Population)

Randomized Treatment Group	Patients (N)	Patients with Events by Day 457 (15 Months) Post Randomization (N)	Day 457 (15-Month) Post Randomization KM Probability	Difference in Proportions	Bootstrap 95% Lower CL	Bootstrap 95% Upper CL	Re-randomization *P*-Value
Omidubicel	62	14	0.25	0.07	-0.09	0.22	0.366
UCBU	63	10	0.18				

Data Source: Listing 16.2.6.2

Abbreviations: CL: Confidence limit; KM: Kaplan-Meier; UCBU: Unmanipulated cord blood unit

Figure 14: Cumulative Incidence of Relapse by 15 Months post Randomization (ITT Population)



Data Source: Listing 16.2.6.2

Note: UCB= Unmanipulated cord blood unit arm

Relapse mortality was assessed at 15 Months post-transplant by both the Kaplan-Meier method and the cumulative incidence method. There was no difference in relapse mortality between groups by either method (Table 14.2.24.1.1, Table 14.2.24.2.1). The cumulative incidence of relapse mortality observed was 13% in the omidubicel arm and 11% in the unmanipulated CBU arm.

With no significant difference in the risk of relapse among the two arms, these results support an overall beneficial risk-benefit ratio for patients randomized to omidubicel.

11.4.6 Immune Reconstitution

Figure 15, Figure 16, Figure 17, Figure 18, and Figure 19 show the counts per liter of different lymphocyte subpopulations at Days 28, 70, 100, 180 and 365 for each treatment group in the AEP population.

In terms of T-cell reconstitution, on Day 28 the unmanipulated CBU group had a higher median level of CD8+ T-cells (23 $\times 10^6$ cells/L vs 14 $\times 10^6$ cells/L, p=0.005) (Table 14.2.25.1). However at later timepoints for CD8+ T-cells, and at all timepoints for CD4+ T-cells counts for omidubicel recipients appear to be at least comparable to unmanipulated CBU.

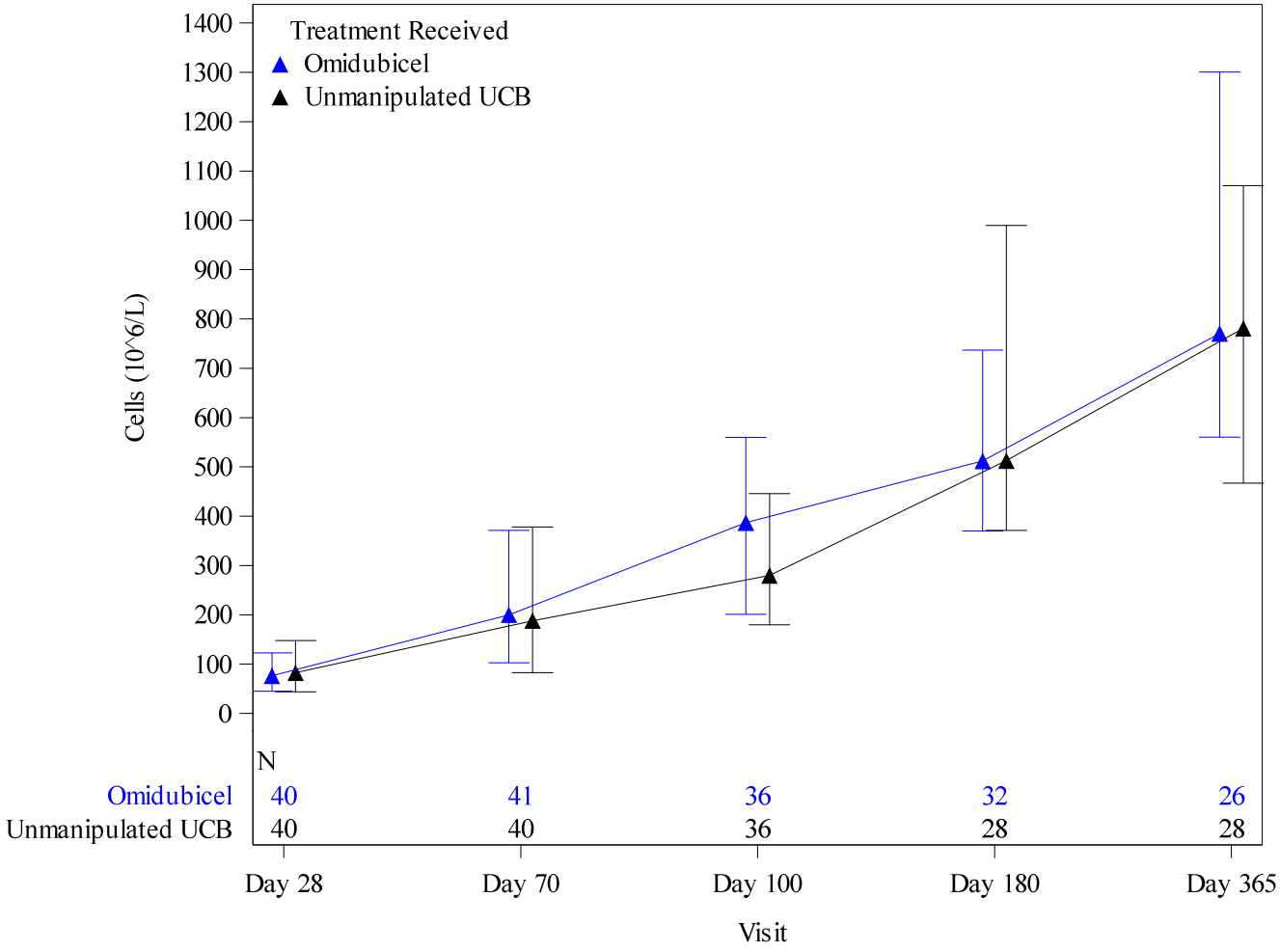
For the B cell recoveries, at Day 28, the omidubicel group had a higher median level of CD19+ B cells (4×10^6 cells/L vs 0×10^6 cells/L, p <0.001). Although later timepoints did not demonstrate significantly higher B cell counts, the curves do appear to numerically separate.

CD56+/CD16+ NK cells were also significantly higher on Day 28 for the omidubicel recipients (311.5×10^6 cells/L vs 82.5×10^6 cells/L, p<0.001) compared to the unmanipulated CBU. The omidubicel group also had a higher median CD56+/CD16+ NK cell count compared to CBU at Day 180 (327×10^6 cells/L vs 245×10^6 cells/L, p=0.07) and Day 365 (408×10^6 cells/L vs 259×10^6 cells/L, p=0.01).

Overall, the recovery of immune cell subsets as reflected by the tests performed in the study centers, indicates that despite the lower CD3+ cell content in the omidubicel grafts, the recovery of CD3+ cells and other subsets is at least comparable to the controls. The recovery of B cells and NK cells may be more robust for omidubicel recipients, which may suggest an explanation for the improved infectious disease outcomes, specifically viral infections.

As noted, these results were obtained from tests analyzed in the individual transplant centers, in different labs and under different processing and analysis protocols, and thus their interpretation is limited. Patient samples were collected for analysis of immune recovery in a central lab and will be reported in a subsequent analysis.

Figure 15: Immune Reconstitution (AEP)- CD3+

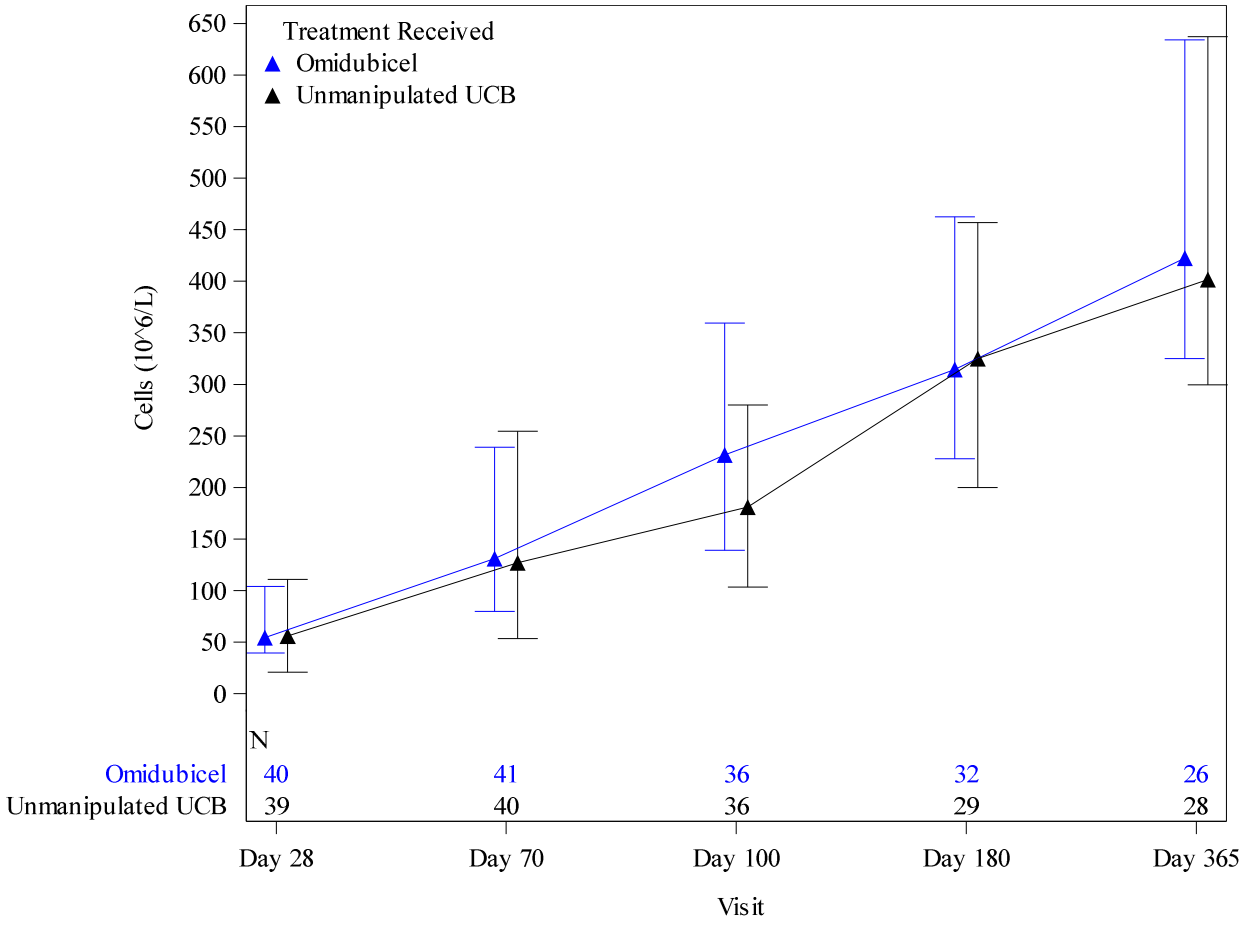


Data Source: Listing 16.2.6.4

Note: Median values are represented by triangles and interquartile ranges are represented by vertical lines at each visit for each treatment group.

Unmanipulated UCB= Unmanipulated cord blood unit treatment group

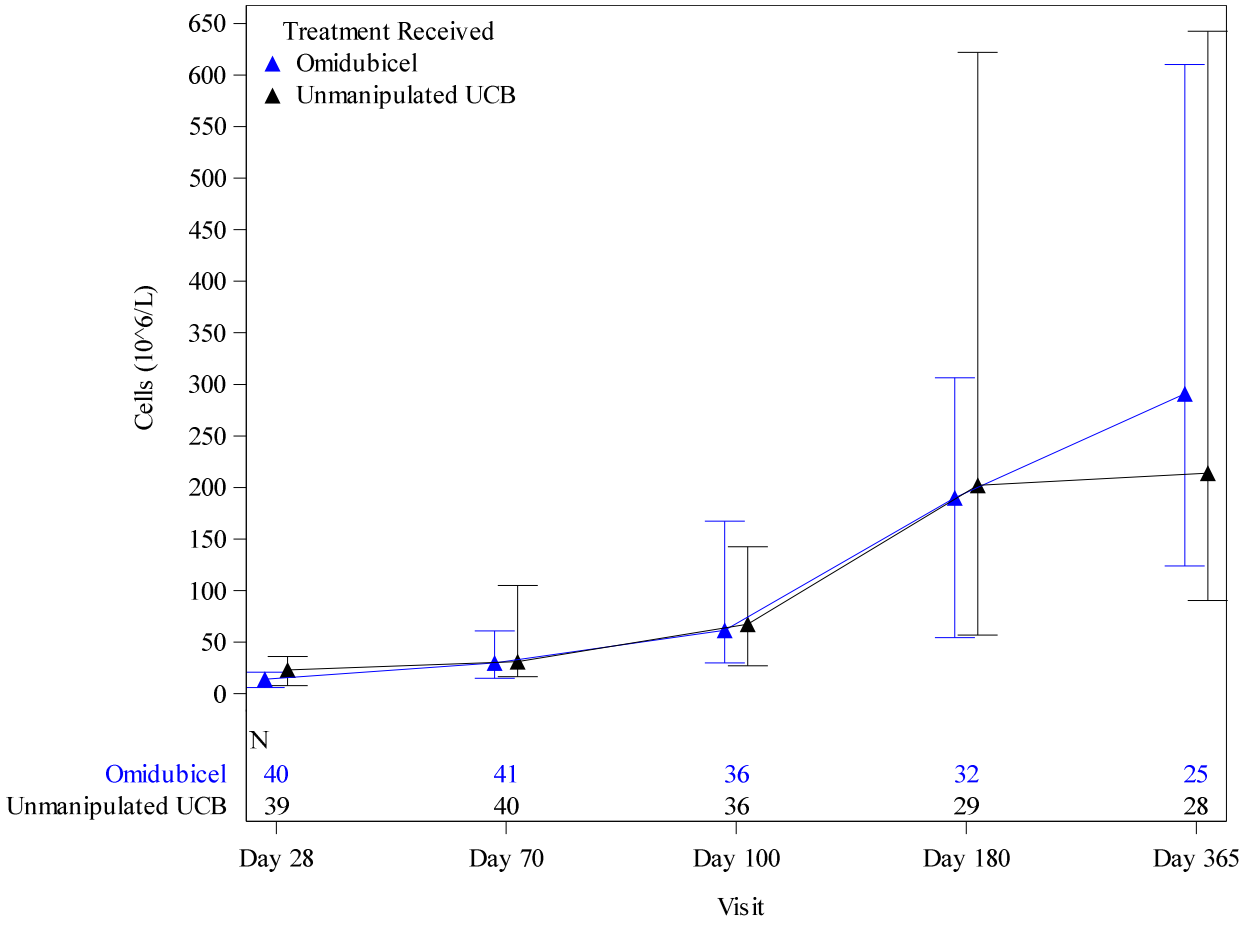
Figure 16: Immune Reconstitution (AEP)- CD4+



Data Source: Listing 16.2.6.4

Note: Median values are represented by triangles and interquartile ranges are represented by vertical lines at each visit for each treatment group.
Unmanipulated UCB= Unmanipulated cord blood unit treatment group

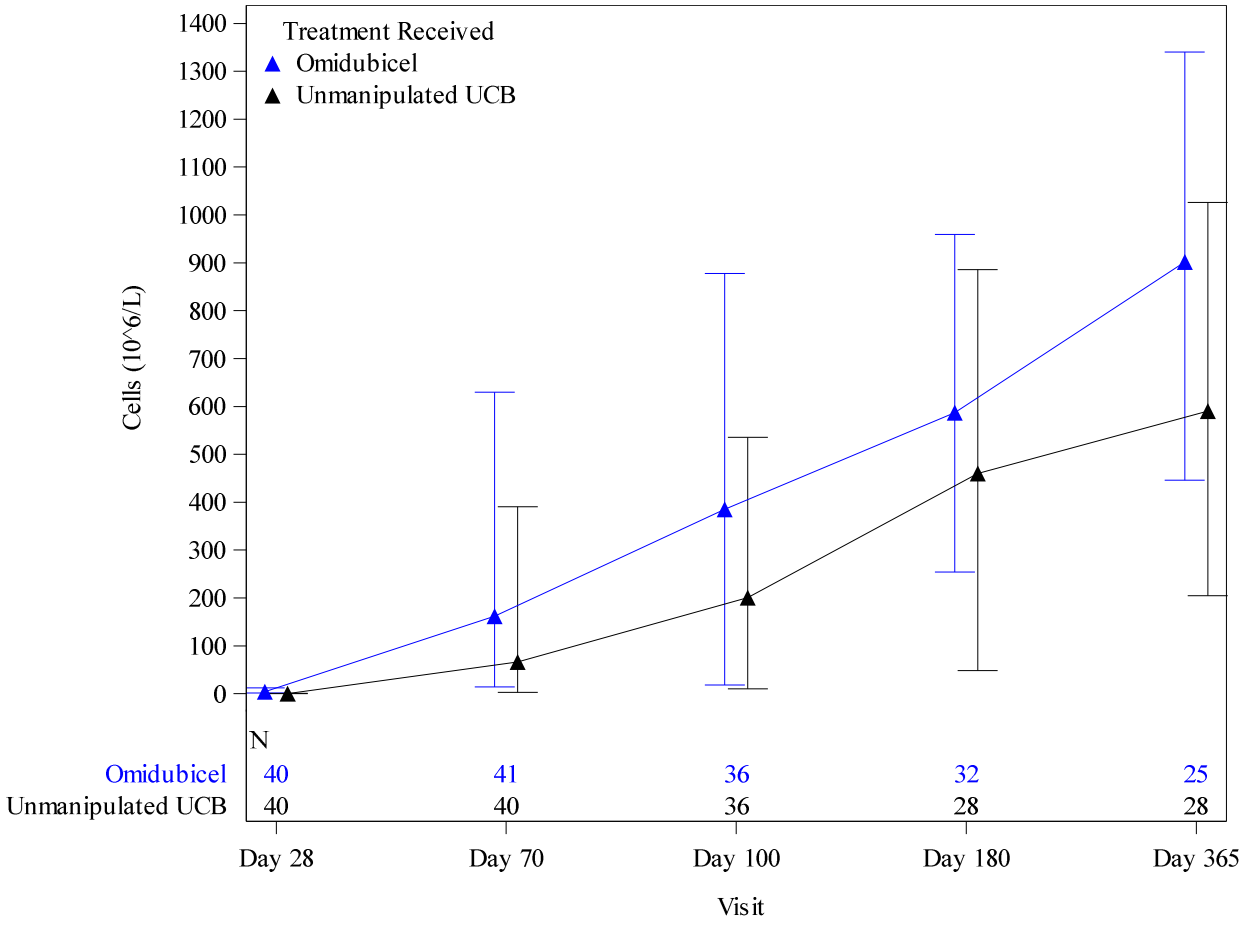
Figure 17: Immune Reconstitution (AEP)- CD8+



Data Source: Listing 16.2.6.4

Note: Median values are represented by triangles and interquartile ranges are represented by vertical lines at each visit for each treatment group.
Unmanipulated UCB= Unmanipulated cord blood unit treatment group

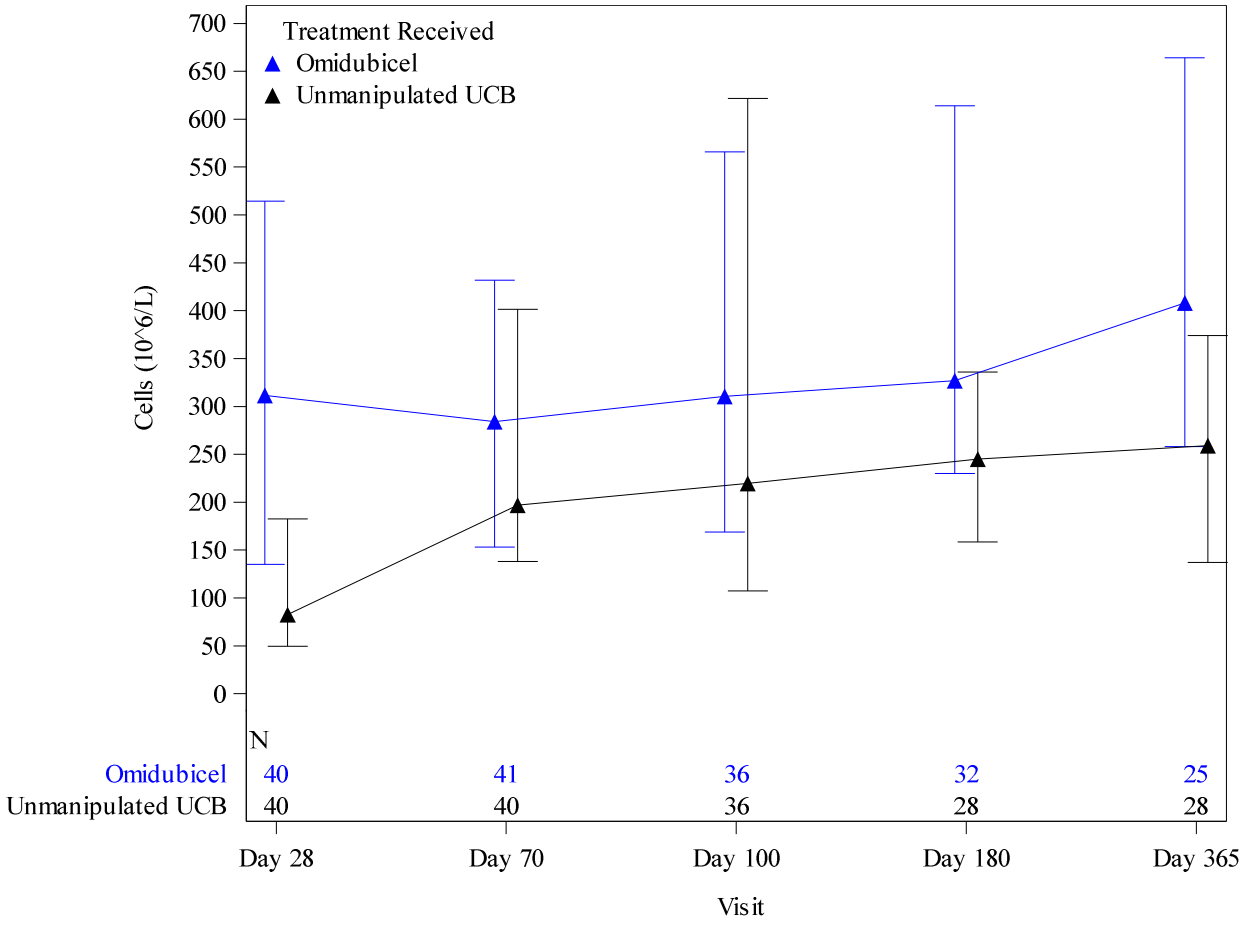
Figure 18: Immune Reconstitution (AEP)- CD19+



Data Source: Listing 16.2.6.4

Note: Median values are represented by triangles and interquartile ranges are represented by vertical lines at each visit for each treatment group.
Unmanipulated UCB= Unmanipulated cord blood unit treatment group

Figure 19: Immune Reconstitution (AEP)- CD56+/CD16+



Data Source: Listing 16.2.6.4

Note: Median values are represented by triangles and interquartile ranges are represented by vertical lines at each visit for each treatment group.
Unmanipulated UCB= Unmanipulated cord blood unit treatment group

11.4.7 Health-Related Quality of Life

Table 14.2.26.1.1, Table 14.2.26.1.2, Table 14.2.26.1.3, and Table 14.2.26.2.1 show the distribution of scores by treatment arm on the FACT-BMT and EuroQol EQ-5D at screening and at Days 42, 100, 180, and 365.

For the EQ5D visual acuity score (patients' overall assessment on a scale of 1-100), patients randomized to omidubicel scored higher on quality of life at all post-transplant visits through Day 365. Omidubicel patients scored better than unmanipulated CBU patients in the EQ5D score of anxiety/depression over the same time period. Omidubicel patients also scored better than unmanipulated CBU patients on EQ5D scores of mobility and self-care through Day 180 but not Day 365. Omidubicel patients scored better in usual activities at Day 42 and Day 100 but not at Day 180 or Day 365 and scored better in pain/discomfort at Day 100 and Day 180 but not at Day 42 nor Day 365. None of these differences were tested for statistical significance.

For the FACT-BMT, patients randomized to omidubicel scored higher on the FACT-G score (an assessment of physical/social/emotional/functional well-being), the BMT specific QoL score, as well as the trial outcomes index (combining BMT score and physical/functional well-being) at all post-transplant visits through Day 365. None of these differences were tested for statistical significance.

11.4.7.1 Post Hoc Exploratory Analyses of Health-Related Quality of Life

Patients included in the as-treated population of the trial who had data on HRQoL measures at both baseline and at least one follow-up visit in the April 2021 data cut were included in this analysis (AnalysisGroup 2021, AnalysisGroup 2021). This analysis focused on five HRQoL outcomes: FACT-G (in the context of FACT-BMT) domain scores for physical well-being, social/family well-being, emotional well-being, functional well-being, and the EQ-5D-3L index score. Rates of missing data were assessed for each HRQoL outcome by treatment group and study visit. Mixed effect models with repeated measures (MMRM) were used to analyze changes from baseline for each measure. Mean change from baseline was modeled as a function of time from baseline (categorical by visit), treatment group (omidubicel vs unmanipulated CBU), the interaction between time and treatment group, baseline value of the HRQoL measure, age, sex, race, region, primary diagnosis, and HCT grade. The covariance among patients' repeated measures during the trial was modeled using an unstructured covariance matrix. Model-based estimates for the mean change from baseline in each group were calculated at Day 42, Day 100, Day 180 and Day 365 post-transplant. An integrated assessment of treatment effects on HRQoL across all of these time points was made by comparing the area under the curve (AUC) of the mean HRQoL change trajectory between treatment groups.

Data from 75 patients (omidubicel n=37, unmanipulated CBU n= 38) who had valid FACT-BMT total scores at both baseline and at least one post-transplant follow-up visit were included in these analyses. These patients were representative of the full randomized population (N=125) at baseline. At baseline, there were no statistically significant differences between the omidubicel and unmanipulated CBU groups in demographics, clinical measures or HRQoL measures. The percentages of patients with missing outcome data on FACT-G domain scores were 19%, 16%, 32% and 39% at Days 42, 100, 180 and 365 post-transplant, respectively. The percentages of patients with missing data on EQ-5D index score was 23%, 24%, 39% and 60% Days 42, 100, 180 and 365 post-transplant, respectively. For all five HRQoL outcomes, the percentage of

patients with missing outcome data was similar between treatment groups at Day 42, and higher in the unmanipulated CBU group than in the omidubicel group at Days 100, 180 and 365.

Physical well-being (Figure 20)
Both the omidubicel and unmanipulated CBU groups had initial numerical declines in mean physical well-being scores between baseline and Day 42, followed by subsequent mean improvements over the rest of the follow-up period. Declines in the first 42 days were numerically smaller in the omidubicel group (mean change = -4.8 units) than in the unmanipulated CBU group (-6.3 units), while mean improvements after Day 42 were greater in the omidubicel group than in the unmanipulated CBU group. On average, relative to baseline, patients in the omidubicel group had numerically improved physical well-being scores by Day 180 (+0.7 units) that were maintained on average at day 365 (+1.2 units). Patients in the unmanipulated CBU group remained numerically worse, on average, relative to baseline at Days 100, 180 and day 365 (mean changes between -2.8 and -1.3 units). When considering the entire trajectory of physical well-being over time, the omidubicel group experienced superior average physical well-being compared to the unmanipulated CBU group (p-value for difference in AUCs = 0.02).

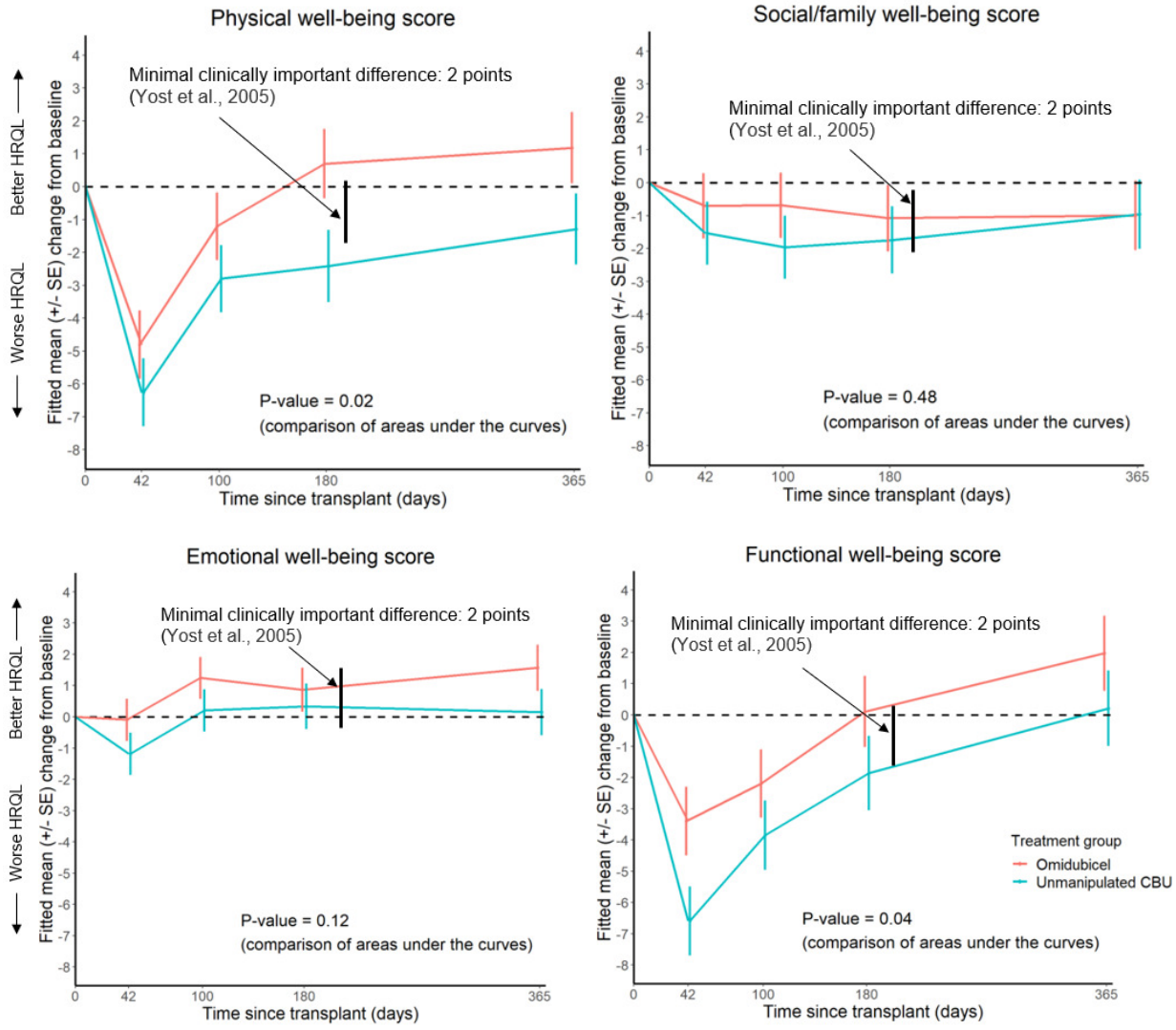
Social/family well-being (Figure 20)
Both the omidubicel and unmanipulated CBU groups had initial numerical declines in mean social/family well-being scores between baseline and Day 42. In the omidubicel group, mean change from baseline at days 100, 180 and 365 were similar to Day 42 (between -0.7 and -1.1 units). In the unmanipulated CBU group, mean declines were greater until Days 42 and 100 with small mean improvements thereafter. In both groups, on average, social/family well-being scores were numerically worse at Day 365 than at baseline (-1.0 unit in both groups). When considering the entire trajectory of social/family well-being over time, differences between the omidubicel and unmanipulated CBU groups on average social/family well-being scores were not statistically significant (p-value for difference in AUCs = 0.48).

Emotional well-being (Figure 20)
Both the omidubicel and unmanipulated CBU groups had initial numerical declines in mean emotional well-being scores between baseline and Day 42, followed by subsequent mean improvements over the rest of the follow-up period. Declines in the first 42 days were numerically smaller in the omidubicel group (mean change = -0.1 units) than in the unmanipulated CBU group (mean change = -1.2 units). On average, relative to baseline, patients in both groups had numerically improved emotional well-being scores at Days 100, 180 and 365, with improvements being numerically greater in the omidubicel group (+0.9 to +1.6 units) than in the unmanipulated CBU group (+0.2 to +0.3 units). When considering the entire trajectory of emotional well-being over time, differences between the omidubicel and unmanipulated CBU groups on average emotional well-being scores were not statistically significant (p-value for difference in AUCs = 0.12)

Functional well-being (Figure 20)
Both the omidubicel and unmanipulated CBU groups had initial numerical declines in mean functional well-being scores between baseline and Day 42, followed by subsequent mean improvements over the rest of the follow-up period. Declines in the first 42 days were numerically smaller in the omidubicel group (mean change = -3.4 units) than in the unmanipulated CBU group (mean change = -6.6 units). Differences between the groups remained

at subsequent time points. On average, relative to baseline, patients in the omidubicel group had regained their baseline mean functional well-being scores by Day 180 (+0.1 units) and numerically improved relative to baseline by Day 365 (+2.0 units). On average, patients in the unmanipulated group returned to the baseline function by Day 365 (mean change = +0.2 units). When considering the entire trajectory of functional well-being over time, the omidubicel group experienced superior average functional well-being compared to the unmanipulated CBU group (p-value for difference in AUCs = 0.04).

Figure 20: Changes from baseline in FACT-G domains

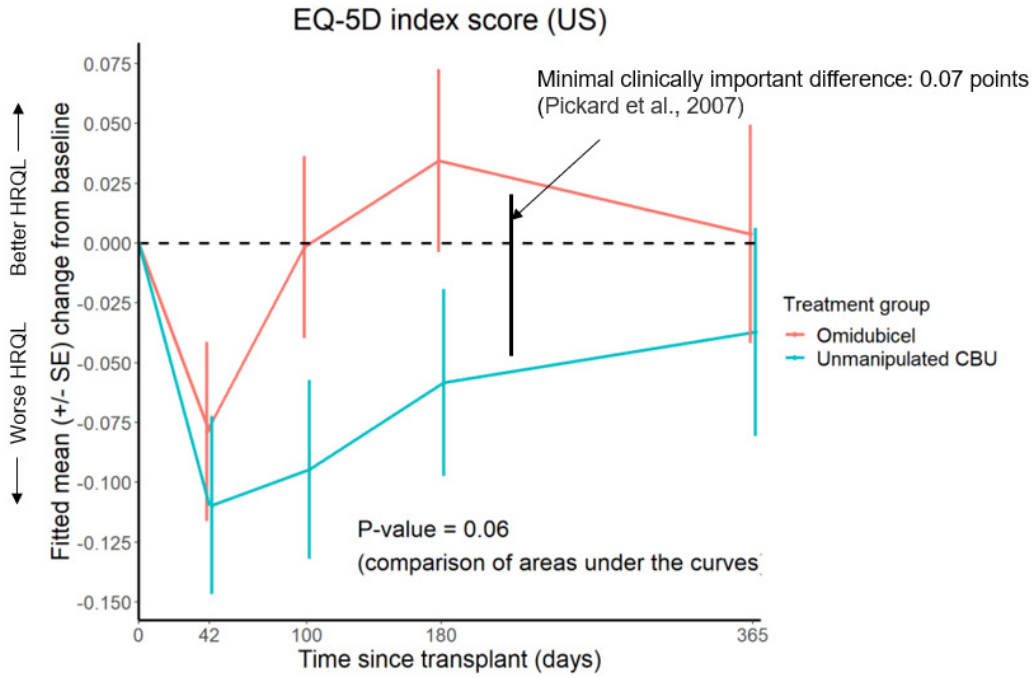


EQ-5D-3L index score (Figure 21)

Both the omidubicel and unmanipulated CBU groups had initial numerical declines in mean EQ-5D-3L index score between baseline and Day 42, followed by subsequent mean improvements over the rest of the follow-up period. Declines in the first 42 days were numerically smaller in the omidubicel group (mean change = -0.08 units) than in the unmanipulated CBU group (mean change = -0.11 units), while mean improvements after Day 42

were greater in the omidubicel group than in the unmanipulated CBU group. On average, relative to baseline, patients in the omidubicel group had regained baseline level of EQ-5D-3L index score by day 100 and maintained this thereafter (+0.00 to +0.03 units). Patients in the unmanipulated CBU group remained numerically worse, on average, relative to baseline at all subsequent time points (-0.04 to -0.09 units). When considering the entire trajectory of EQ-5D-3L index score over time, differences between the omidubicel and unmanipulated CBU groups were not statistically significant (p-value for comparison of AUCs between groups = 0.06).

Figure 21: Change from baseline in EQ-5D-3L index scores



11.4.8 Statistical/Analytical Issues

11.4.8.1 Adjustment for Covariates

None of the primary analyses were adjusted for covariates. A secondary analysis of the primary endpoint stratified by disease was performed and the results are provided in Table 14.2.1.6.1. In this analysis, a stratified Mann-Whitney test of the primary endpoint was conducted using the ITT population. There were six strata according to disease Type (AML, ALL, CML, MDS, lymphoma, and other); the test statistic was the stratified Mann-Whitney test (otherwise known as the van Elteren test); the p-value was computed using the rerandomization test. The results were consistent with the primary analysis finding of shorter time to neutrophil engraftment in the omidubicel group.

11.4.8.2 Handling of Dropouts or Missing Data

There were no dropouts or missing data related to the primary or secondary endpoint analyses.

All cumulative incidence curves presented in this report incorporate adjustment for competing risks. For the primary endpoint analysis, failure to receive a cord transplant within 90 days of

randomization was considered a competing risk. Death, second transplant, and relapse prior to neutrophil recovery were also considered competing risks. All competing risks were assigned as Day 43 in the primary endpoint analysis, the same value given to primary graft failures.

For the secondary endpoint of platelet engraftment, patients not receiving transplant within 90 days following randomization or dying or relapsing before platelet engraftment were counted as not having engrafted.

For the secondary endpoint of incidence of Grade 2/3 bacterial infection or invasive fungal infection, death was considered a competing risk.

For the secondary endpoint of days alive and OOH, patients who did not receive a transplant within 90 days following randomization were assigned a value of 0 days alive and OOH.

11.4.8.3 Multicenter Studies

There are insufficient numbers of patients at each clinical site to make an analysis of individual site results informative. Subgroup analyses by geographical region are described in Section 14.

11.4.8.4 Multiple Comparison/Multiplicity

All statistical tests were conducted against a two-sided alternative hypothesis, employing a significance level of 0.05. For the secondary endpoints, p-values were adjusted for multiple testing using Hommel's method that controls the family-wise error (FWE) rate. After adjustment of p-values for the multiple comparisons involved in examining three secondary endpoints, the advantage to omidubicel over unmanipulated CBU was demonstrated to reach the critical level of significance (0.05) on all three endpoints (Table 24).

Table 24: Multiple Comparison Adjustments

Secondary Endpoint	Original *P*-Value in ITT Population	Hommel *P*-Value
Days Alive and Out of Hospital By Day 100 Post-transplant	0.005	0.014
Cumulative Incidence of First Grade 2/3 Bacterial or Invasive Fungal Infection	0.016	0.028
Platelet Engraftment by Day 42 Post-Transplant	0.028	0.028

Data Source: Table 14.2.5.1
Abbreviation: ITT: Intent-to-treat population

The results of the tertiary and exploratory endpoints were assessed to provide a broad picture of the efficacy and safety of omidubicel in comparison with unmanipulated CBU transplant. However, tests of these endpoints were not adjusted for multiple comparisons.

P-values were also not adjusted for the multiple analyses performed on the 1-year or later endpoints. These longer-term endpoints were formally evaluated twice; once after all patients were followed through 180 days post-transplant, and subsequently after all patients completed their study follow-up.

11.4.8.5 Use of an Efficacy Subsets of Patients

All of the primary analyses for the primary, secondary, and tertiary endpoints, as well as the majority of exploratory endpoints were conducted on all randomized patients (ITT population) using all available data. The same analyses were also conducted on alternative populations (TP, AT, AEP, PEP) as defined in Section 11.1. These additional analyses resulted in similar outcomes with no substantial differences in results, demonstrating the robustness of the principal trial conclusions.

11.4.8.6 Active Control Studies Intended to Show Equivalence

Not applicable.

11.4.8.7 Examination of Subgroups

Descriptive statistics were calculated based on the primary analyses of the primary and secondary endpoints for the following subgroups; disease risk group, age group, intention to perform single versus double CB transplant, disease, HCT-specific Comorbidity Index, gender, race/ethnicity, and geographical region. P-values were not calculated for any of the comparisons due to the small sample sizes and interpretability of results. These are provided in Table 14.2.1.8.1 (neutrophil engraftment by age and gender), Table 14.2.1.8.2 (neutrophil engraftment post hoc analysis), Table 14.2.2.1.5 (incidence of infection), Table 14.2.3.4.2 (time alive and OOH), and Table 14.2.4.5.2 (platelet engraftment). While the small sample sizes limit the review, inspection of these descriptive statistics did not reveal any trends indicative of substantive differences in these endpoints between subgroups.

A summary of key demographic and disease subgroups demonstrates that the differences in the time to neutrophil engraftment among the omidubicel and the unmanipulated CBU arms were generally consistent considering the small numbers in each subgroup. In terms of patient gender, the differences in median time to neutrophil engraftment between the arms were 13 days for males and five days for females. In the age subgroups, the differences in median time to neutrophil engraftment between the arms were 14 days for the 12-17 age group, 11 days for the 18-39 age group, and six days for the 40-65 age group. Geographically, the differences in median time to neutrophil engraftment between the arms were ten days for US patients, ten days for European patients and ten days for patients in other countries.

In the disease subgroups, the differences in median time to neutrophil engraftment between the arms were 12 days for the ALL subgroup, seven days for AML, 14 days for CML, ten days for MDS, and 15 days for lymphoma. In terms of disease risk, the differences in median time to neutrophil engraftment between the arms were six days for low risk disease, seven days for moderate risk and 14 days for high/very high-risk.

11.4.9 Tabulation of Individual Response Data

Individual efficacy measurements are presented in Listing 16.2.6.

11.4.10 Drug Dose, Drug Concentration, and Relationships to Response

This section analyzes the cell doses administered to omidubicel and unmanipulated CBU recipients, as encompassed by the total nucleated cell counts and doses, CD34+ cells counts and doses, and CD3+ cell counts and doses. Any potential relationships of cell doses to response, primarily neutrophil engraftment, are discussed. Patients who received grafts with cellular parameters that did not meet the protocol or product requirements are discussed. In addition, HLA matching of the graft to the recipient are also discussed, as an additional important parameter characterizing the graft.

Table 25: Graft Characteristics: CBUs Selected Prior to Randomization Using Pre-Cryopreservation Data Provided by the Cord Blood Banks (ITT Population)

			Randomized to UCBU					
	Randomized to Omidubicel[a]		UCBU (Unit 1)[a]		UCBU (Unit 2)[b]		UCBU (Total)	
	N	Median (Range)	N	Median (Range)	N	Median (Range)	N	Median (Range)
Weight used for CBU selection (kg)	62	77 (43-132)	63	76 (49-135)	42	83 (49-135)	63	76 (49-135)
Total nucleated cell count ($\times 10^9$ cells)	62	2.3 (1.8-5.4)	63	2.5 (1.8-4.1)	42	2.2 (1.1-4.1)	63	4.0 (1.8-7.1)
Total nucleated cell dose ($\times 10^7$ cells/kg)[c]	62	3.3 (1.6-9.9)	63	3.4 (1.9-7.0)	42	2.6 (1.5-5.0)	63	4.8 (2.5-9.6)
Viability (%)	58	98 (82-100)	58	98 (73-100)	39	97 (85-100)	55	97 (85-100)
Total CD34+ cell count ($\times 10^6$ cells)	62	13.8 (8.1-39.6)	63	14.3 (7.8-34.6)	42	12.7 (3.9-29.8)	63	23.9 (10.5-54.9)
Total CD34+ cell dose ($\times 10^6$ cells/kg) [d]	62	0.2 (0.1-0.6)	63	0.2 (0.1-0.5)	42	0.2 (0.1-0.5)	63	0.3 (0.1-1)

Data Source: Listing 16.2.5.3
N= Number of patients included in the median calculation for each category
[a] Based on CBU selected prior to randomization as the Treatment 1 CBU.
[b] Based on CBU selected prior to randomization as the Treatment 2 CBU if intent is to have a double cord infusion.
[c] Doses are calculated based on weight used for CBU selection.
Abbreviations: CBU: Cord blood unit; UCBU: Unmanipulated cord blood unit

Table 26: Graft Characteristics: Grafts Used for Transplantation (AT Population)

	Received Omidubicel				Received UCBU[a]					
	Cord Blood Bank Results		Production Results[b]		UCBU (Unit 1)		UCBU (Unit 2)		UCBU (Total)	
	N	Median (Range)	N	Median (Range)	N	Median (Range)	N	Median (Range)	N	Median (Range)
Weight for CBU selection (kg)	52	80 (43-132)	52	80 (43-132)	56	73 (49-135)	37	73 (49-135)	56	73 (49-135)
Total viable nucleated cell count ($\times 10^9$ cells)	48	2.2 (1.6-3.4)	52	3.9 (1.2-10.2)	47	1.6 (0.5-3.2)	32	1.6 (0.6-3.7)	47	2.9 (0.8-6.5)
Total viable nucleated cell dose ($\times 10^7$ cells/kg)[c]	48	2.9 (1.8-6.9)	52	4.7 (1.7-12.4)	47	2.2 (0.9-4.0)	32	1.9 (0.9-4.1)	47	3.4 (1.3-8.0)
Total CD34+ cell count ($\times 10^6$ cells)	52	14.0 (8.6-39.6)	52	655 (280-3900)	42	11.1 (0.2-45.9)	29	8.2 (0.3-28.8)	42	15.8 (0.2-46.4)
Total CD34+ cell dose ($\times 10^6$ cells/kg)[d]	52	0.2 (0.1-0.5)	52	9.0 (2.1-47.6)	42	0.2 (0.0-0.8)	29	0.1 (0.0-0.4)	42	0.2 (0.0-0.8)
Total CD3+ cell count ($\times 10^6$ cells)	NAV	NAV	52	210 (71–640)	25	292 (4.4-829)	13	238 (6.0-380)	25	413 (4.4-990)
Total CD3+ cell dose ($\times 10^6$ cells/kg)[e]	NAV	NAV	52	3.0 (1.1-12.4)	25	4.0 (0.0-14.8)	13	3.2 (0.1-5.7)	25	4.6 (0.0-14.8)

Data Source: Listing 16.2.5.1
N= Number of patients included in median calculation for each category
[a] Values are from infusion
[b] Certificate of Analysis values; values are from the end of production, prior to cryopreservation because the product is administered in a closed system.
[c] Doses are calculated based on weight used for CBU selection
Abbreviations: CBU: Cord blood unit; NAV: Not available; UCBU: Unmanipulated cord blood unit

Decisions on the selection of CBUs are based on specific histocompatibility data, cell dose, availability, and in some cases the source of the CBU. Eligible CBUs for the study were required to meet HLA match and cellular requirements. However, the protocol did not specify prioritization rules when more than one eligible CBU was identified.

The cellular requirements for CBU selection focused on the total nucleated cells and the CD34+ cells, reflecting the stem and progenitor cell population. The CBU intended for expansion (Treatment CBU #1) was required to contain a total CD34+ cell count of at least 8×10^6, as well as a total nucleated cell count of at least 1.8×10^9, and a total nucleated cell dose of at least 1.5×10^7 total nucleated cells/kg.

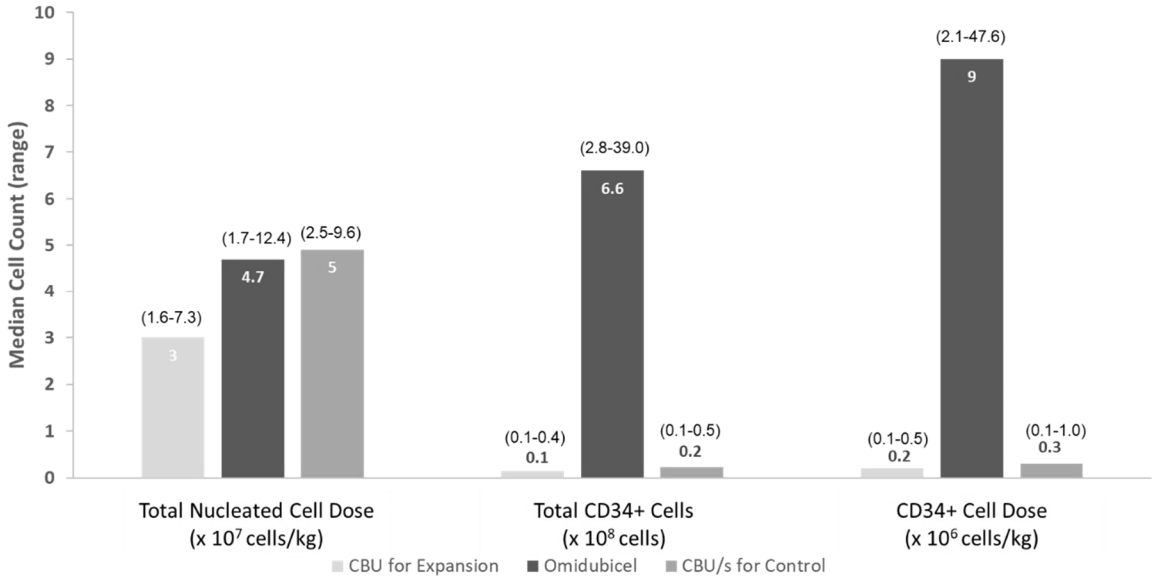
For the unmanipulated CBU group, CBU #1 met the same criteria, as CBU selection was done prior to randomization. In cases where the cellularity and HLA match of CBU #1 did not meet the protocol-specified criteria for a single unmanipulated CBU transplantation, a second CBU was added for a double unmanipulated CBU transplantation. The second CBU was required to have sufficient cellularity so that the combined total nucleated dose of the two CBUs would be at least 3×10^7 TNC/kg.

HLA match scores for the ITT and AT populations are presented in Table14.1.12 and Table 14.1.12.2. Table 14.1.15 and Table 14.1.16 provide the CBU characteristics for the ITT and AT populations. As shown, the HLA match and cellularity parameters (TNC, TNC/kg, CD34, CD34/kg) for CBU #1 were similarly distributed among the treatment groups in both the ITT population and the AT population.

Table 25 shows the CBU characteristics for the CBUs selected for omidubicel and unmanipulated CBU, as reported by the CBBs. Data are provided on total TNC and CD34+ cells counts, as well as the cell doses per patient kg. As can be seen, the CBUs selected for the unmanipulated CBU group contained a higher total cellular count/dose (TNC and CD34) because approximately two thirds of the patients were treated with a double CBT. Table 26 shows the characteristics of omidubicel or the unmanipulated CBU grafts that were transplanted, according to the graft that was actually infused. The counts for the unmanipulated CBU group were taken at infusion, while the counts for omidubicel were taken at the end of manufacturing, prior to cryopreservation. In addition to TNC and CD34+, data of CD3+ lymphocyte cell counts and doses are also provided.

As demonstrated in Figure 22, the total nucleated cell counts following expansion are only about 1.5-fold higher than the CBU TNC counts, either in comparison to the CBUs selected for omidubicel, or in comparison to the CBUs selected for unmanipulated CBU transplantation. However, the total CD34 counts of omidubicel following expansion are approximately 45-fold higher than the CD34 counts of the CBU before expansion, or of the unmanipulated CBUs, demonstrating the stem and progenitor cell enrichment afforded by the expansion process. Patients treated with omidubicel received a graft containing a median of 9.0×10^6 CD34 cells/kg, compared to 0.3×10^6 CD34 cells/kg in the patients treated with unmanipulated CBU. Thus, although the total nucleated cell doses of omidubicel are similar to unmanipulated CBU, omidubicel recipients received a substantially higher dose of CD34+ cells than unmanipulated CBU, a dose that is quantitatively similar to CD34+ doses infused in peripheral blood donor transplants (Anasetti, Logan et al. 2012).

Figure 22: Omidubicel and Unmanipulated CBU Graft Characteristics

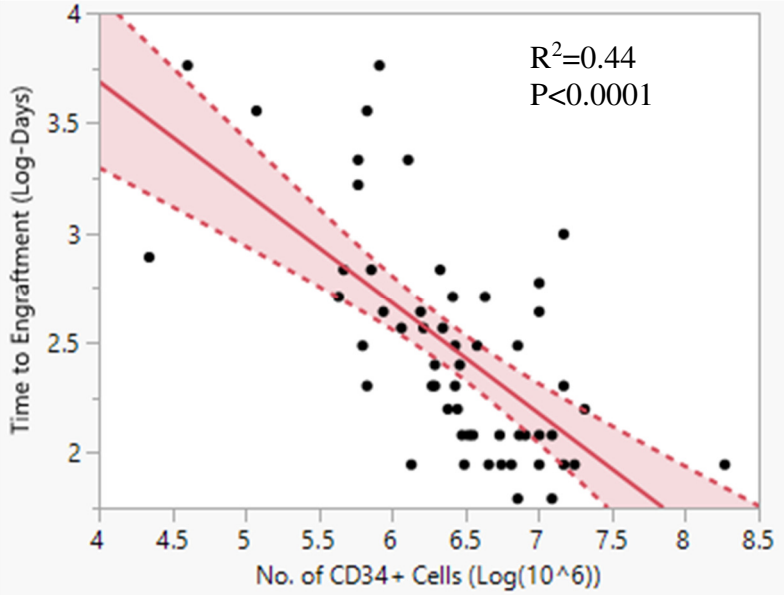


Data Source: Listing 16.2.5.1, Listing 16.2.5.3, Listing 16.2.5.4

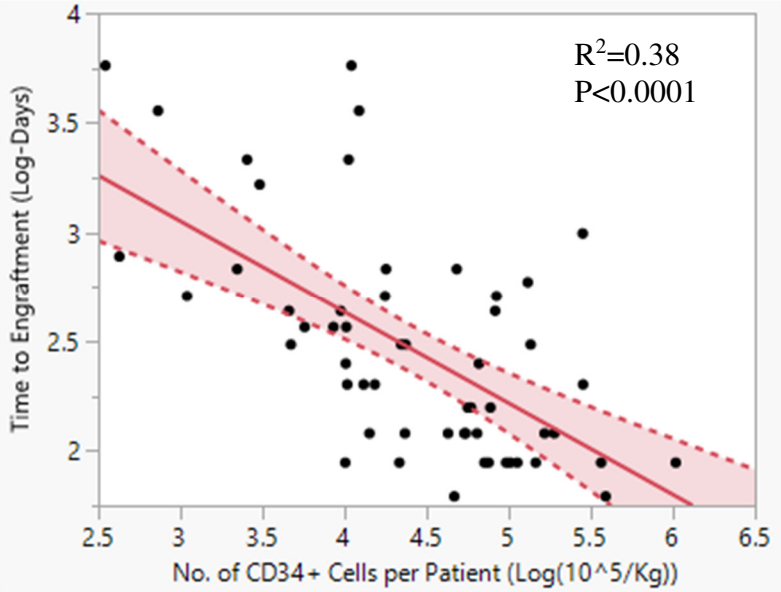
The apparent contribution of the expansion process is in line with the faster hematopoietic recovery observed in patients treated with omidubicel. The CD34+ dose infused to patients has been shown to correlate with neutrophil engraftment – higher infused CD34+ doses lead to more rapid neutrophil engraftment (Purtill, Smith et al. 2014). Analyses correlating the cellularity of omidubicel to the time to neutrophil engraftment demonstrate a strong correlation of the CD34+ total cell counts in omidubicel, and the CD34+ cell dose/kg with the kinetics of neutrophil recovery, demonstrating that higher CD34+ counts and doses are associated with a more rapid neutrophil recovery following omidubicel transplantation. Figure 23 demonstrates analyses performed on patients transplanted with omidubicel on the study: (A) Regression of the time to engraftment on the total number of CD34+ cells (both on the natural logarithmic scale). The shaded interval is the pointwise 95% confidence interval around the predicted log time. The regression line is log days to engraftment = 5.70 - 0.50 log (10^6 total cells) (r=-0.66, p<0.001); and (B) Regression of the time to engraftment on the number of CD34+ cells per patient weight (both on the natural logarithmic scale). The shaded interval is the pointwise 95% confidence interval around the predicted log time. The regression line is log days to engraftment = 4.30 – 0.42 log (10^5 cells/kg) (r=-0.62, p<0.001). These analyses included all patients exposed to omidubicel (n=56), including 52 patients on the omidubicel AT population, three patients transplanted with omidubicel that did not meet release specifications, and one patient transplanted with omidubicel after the protocol allowed interval of 90 days from randomization to transplantation.

Figure 23: Correlation of CD34+ Total Cell Count and Cell Dose with Time to Neutrophil Engraftment of Omidubicel

A.



B.



Data Source: (PharmaLex 2021)

On the other hand, patients treated with omidubicel were infused with a lower number, and lower dose of CD3+ lymphocyte cells. The CD3+ lymphocytes in omidubicel are entirely derived from the omidubicel NF. As a result of the manufacturing process manipulations and freeze-thaw cycles, the CD3+ dose of the omidubicel NF is lower than in a unmanipulated CBU transplantation. The median CD3+ cell dose in omidubicel was 3×10^6 cells/kg, compared to 4.6×10^6 cells/kg in the unmanipulated CBUs. The median CD3+ cell count in omidubicel was 210×10^6 cells/kg, compared to 413×10^6 cells/kg in the unmanipulated CBUs. Of note, the infused CD3+ cell dose for omidubicel cannot be directly measured, and the cell numbers were

based on counts performed at the end of manufacturing, prior to re-cryopreservation. Based on experience accumulated during product development, which demonstrated a median 70% recovery after omidubicel NF thawing, it can be estimated that the CD3+ cell numbers infused were approximately 30% lower.

Although a lower infused lymphocyte dose may have been associated with impaired immune system recovery, the study data did not raise any concerns. Immune reconstitution data from omidubicel transplantation demonstrated multilineage recovery of immune cells in the weeks following transplant, which was at least comparable to the unmanipulated CBU group (Section 11.4.6). These results indicate that the lower CD3+ dose in omidubicel did not increase the risk of impaired immune recovery following transplantation. Furthermore, outcomes of viral infections up to a year following omidubicel transplantation demonstrated an advantage for omidubicel treatment, and relapse – related outcomes demonstrated no difference from unmanipulated CBU transplantation (Sections 11.4.3.2 and 11.4.5.4). Thus, there appears to be no impact on safety as a result of the lower CD3+ dose in omidubicel.

Table 27: CBU and Omidubicel HLA Matching to the Patient (AT Population)

	Omidubicel (N=52)	**UCBU #1 (N=56)**	**UCBU #2 (N=37)**
Antigen-level HLA match score			
4/6	37 (71.2%)	42 (75.0%)	29 (78.4%)
5/6	14 (26.9%)	13 (23.2%)	7 (18.9%)
6/6	1 (1.9%)	1 (1.8%)	1 (2.7%)
Allele level HLA match score			
2/8	2 (3.8%)	3 (5.4%)	1 (2.7%)
3/8	5 (9.6%)	6 (10.7%)	2 (5.4%)
4/8	9 (17.3)	16 (28.6%)	8 (21.6%)
5/8	25 (48.1)	24 (42.9%)	14 (37.8%)
6/8	7 (13.5%)	5 (8.9%)	8 (18.9%)
7/8	2 (3.8%)	2 (3.6%)	1 (2.7%)
8/8	1 (1.9%)	0 (0.0%)	1 (2.7%)
Missing	1 (1.9%)	0 (0.0%)	2 (5.4%)

Data Source: Listing 16.2.8.13

Abbreviations: HLA: Human leukocyte antigens; UCBU: Unmanipulated cord blood unit

HLA matching between the patient and the infused stem cell product were similar between the omidubicel and unmanipulated CBU arms for both antigen-level matching (antigen-level matching at A and B locus and allele matching at DRB1) and allele level matching (allele level matching at A, B, C, and DRB1) (Table 27).

Under FDA approval, three patients on the study were transplanted with omidubicel that did not meet the product release specification.

As shown in Table 28, all three omidubicel grafts did not meet the minimal specification for the omidubicel CF total nucleated cell count. However, the CD34+ cell counts were above specifications, and the CD34+ dose per kg justified consideration of infusing the grafts. Overall

outcomes for all the patients transplanted with omidubicel are also provided as a reference for the OOS product results.

Table 28: Omidubicel Characteristics for Products Infused OOS

	Minimal Product Specification	GP3DFC-006	GP3OHS-005	GP3NWU-002	Overall Omidubicel Characteristics in AT Population (N=52) (Median (Range))
Final CF total viable nucleated cells ($\times 10^9$)	0.8×10^9	0.67	0.52	0.65	2.75 (1.1-9.2)
Final CF total viable CD34+ cells ($\times 10^8$)	0.56×10^8	1.6	0.77	1	6.6 (2.8-39.0)
Final CF CD34+ cells/kg ($\times 10^6$)	NA	1.8	1.4	1.2	9.0 (2.1-47.6)
NF total viable nucleated cells ($\times 10^8$)	4×10^8	8.6	9.1	12	9.5 (3.9-21.0)
NF total viable CD3 ($\times 10^8$)	0.24×10^8	2.3	1.6	1.9	1.95 (0.24–6.40)
NF CD3/kg ($\times 10^6$)	NA	2.6	2.8	2.4	3.0 (0.3-12.4)

Data Source: Listing 16.2.5.1, Listing 16.2.5.4

Abbreviations: AT: As treated; CF: Cultured fraction; NA: Not applicable; NF: Non-cultured fraction

The Table 29 below outlines the demographics and baseline characteristics, as well as the main outcomes for the three patients who were infused with OOS omidubicel.

Table 29: Patients transplanted with OOS omidubicel

Patient ID	Demographics	Baseline Characteristics	Time to Neutrophil Engraftment (Days)	Time to Platelet Engraftment (Days)	Safety Events
GP3DFC-006	White Male 51 yo	- ALL High/very high-risk - Five prior chemotherapy cycles (including intrathecal treatment) - 3+ Comorbidity Index - Moderate pulmonary impairment at screening	35	46	- Five Grade 2/3 bacterial infections (including blood and respiratory infection) - Pneumonitis SAE at 108 days post-transplant, following a gradually progressive worsening of the patient's pulmonary status - Patient died 288 days post-transplant (pulmonary organ failure)
GP3OHS-005	White Female 56 yo	AML low risk	18	45	- Grade II acute GvHD - Alive at last study follow-up (day 419 post-transplant)
GP3NWU-002	Asian Male 32 yo	AML moderate risk	Primary Graft Failure	NA	- Initial pre and pos-transplant periods complicated with *C. Difficile* infection (treated with vancomycin), BK viruria and HHV6 viremia (treated with foscarnet) - Underwent second transplant from haploidentical donor after 36 days, with subsequent engraftment - In parallel to the second transplant: sepsis followed by secondary graft failure - Patient received two additional haploidentical CD34+ cell infusions with intercurrent infectious episodes - Patient relapsed on day 134 following the initial transplant - Death reported 180 days following the initial transplant

Data Source: Listing 16.2.4.5

Abbreviations; ALL: Acute lymphoblastic leukemia; AML: Acute myelogenous Leukemia; GvHD: Graft-versus-host disease; HHV6: Human herpesvirus 6; NA: Not available; SAE: Serious adverse event; yo: Years old

The clinical outcomes following omidubicel transplantation which did not meet product specifications were variable. One patient engrafted on Day 18, one on Day 35, and one failed to engraft. The two patients with delayed or failed engraftment had additional potential contributing factors to their overall clinical outcomes including pre-existing organ impairment from prior treatments and intercurrent infections requiring treatment that may have contributed to BM suppression. There is insufficient data to assess the safety risks or benefits for these patients.

Six patients on the study were transplanted with unmanipulated CBUs that did not meet the protocol requirements. The reasons are described in Table 12 and include: Investigator decision not to proceed with the CBU selected prior to randomization (GP3LAF-008, GP3UMN-008), omidubicel manufacturing failure (GP3RMH-001), quality/logistic issues with the pre-selected CBU (GP3UMN-009, GP3KMC-002), and error (GP3CCF-004).

Main outcomes are provided in Table 30. One patient (GP3RMH-001) failed to engraft within 42 days. Of note, a deviation was recorded for the G-CSF treatment for this patient – G-CSF was erroneously held between Day 7 and Day 17 post-transplant, which may have contributed to the impaired engraftment. This patient eventually engrafted 55 days post-transplant. Overall, these results are within the anticipated range for patients transplanted with unmanipulated CBUs.

Table 30: Outcomes of Patients Transplanted with Unmanipulated CBUs that did not Meet Protocol Requirements

Patient ID	Assigned Treatment	Time to Neutrophil Engraftment (Days)	Time to Platelet Engraftment (Days)	Secondary Graft Failure or Relapse Post-Transplant	Death (Days Post-Transplant)
GP3LAF-008	Omidubicel	20	No	Relapse on Day 138	144 (Disease relapse)
GP3UMN-008	Omidubicel	27	48	No	No
GP3RMH-001	Omidubicel	Engraftment Failure	No	No	No
GP3UMN-009	UCBU	30	56	No	No
GP3KMC-002	UCBU	13	No	No	35 (acute hypoxic respiratory failure; infection, viral)
GP3CCF-004	UCBU	27	166	No	182 (Hypoxic respiratory failure; Inflammatory lung disease)

Data Source: Listing 16.2.6.12, Listing 16.2.7.1, Listing 16.2.6.2, Listing 16.2.6.7

Abbreviations: UCBU: Unmanipulated cord blood unit

Eleven patients on Study P0501 were infused with omidubicel using an in-line filter. All the filters utilized had a filter pore size of at least 150 µm. For six patients a 180 µm filter was used, for two patients a 200 µm filter was used, and for two additional patients – a 170 µm filter and a 170-260 µm filter, respectively.

An additional patient (GP3NWU-002) was infused with the omidubicel product with an in-line filter set. The patient is not included in this analysis as the infused product was OOS.

The baseline patient and graft characteristics are displayed in Listing 16.2.4.10 and Listing 16.2.5.5. With a median age of 24 years, the patients were younger than the overall study population, but otherwise had similar demographic, disease and graft characteristics as the overall study patients treated with omidubicel.

Among the 11 patients infused using an in-line filter, all patients engrafted at a median time to neutrophil engraftment of 10 days (range, 7 – 28). Platelet engraftment by Day 180 post-transplant was achieved by 9/11 patients, with 6/11 patients (55%) achieving platelet engraftment by Day 42 post-transplant. Four out of 11 patients (36%) had Grade 2 or 3 bacterial infections during the first 100 days post-transplant. Two out of 11 patients (18%) had disease relapse post-transplant.

Five out of 11 patients (45%) experienced infusion reactions. Three patients had a maximum Grade 1 or 2 infusion reaction, and two patients had maximum Grade 3 infusion reactions. There were no Grade 4 or 5 infusion reactions reported for this group. None of the reactions were reported as related to the study product.

Eight out of 11 patients had acute GvHD in the first 100 days post-transplant. Seven out of 11 patients had Grade II acute GvHD, and 1/11 patients had Grade III acute GvHD.

Three patients (27%) among this group died – one patient died 103 days post-transplant due to a pulmonary alveolar hemorrhage, one patient died 59 days post-transplant due to veno-occlusive liver disease and one patient died 31 days post-transplant due to hyperacute GvHD.

In summary, the post-transplant outcomes for the 11 patients infused using an in-line filter were similar to the outcomes of the overall group of patients treated with omidubicel, demonstrating comparable engraftment and did not demonstrate a safety risk beyond the known safety profile. Although the rates of acute GvHD were higher than observed in the overall study population, the small numbers in this subgroup do not allow for any definitive conclusion.

11.4.11Drug-Drug and Drug-Disease Interactions

Not applicable.

11.4.12 By-Patient Displays

Individual efficacy measurements are presenting via data listings in Appendix 16.2.

11.4.13 Efficacy Conclusions

Patients randomized to receive either omidubicel or unmanipulated CBU transplantation were followed for post-transplant outcomes reflected in the study primary, secondary and exploratory endpoints. The primary and secondary efficacy endpoints were analyzed on the ITT populations, in order to account for all patients treated on the study, as well as patients who were not

transplanted. As such, the efficacy analyses encompass a comprehensive assessment of omidubicel efficacy. The study exploratory endpoints further assessed the effects of omidubicel on engraftment, looking also at the AT population, including those patients who were treated according to the protocol requirements.

The study included adolescent and adult patients aged 12-65 years, with an array of hematologic malignancies in need of allogeneic HSCT. Importantly, the racial and ethnic diversity of the patients enrolled on the study reflects the unmet need of these patient populations for a transplant donor option with effective results.

The study met its primary endpoint, demonstrating by ITT analysis that the time to engraftment was shortened by omidubicel transplantation compared to unmanipulated CBT ($p<0.001$). Patients in the omidubicel group reached neutrophil engraftment 10 days earlier than patients in the unmanipulated CBU group, at a median time of 12 days (95% CI 10-14). Multiple secondary sensitivity analyses support the overall conclusions from the primary endpoint analyses as results regarding time to neutrophil engraftment were consistent.

In the AT population, 96% of patients who received omidubicel achieved successful neutrophil engraftment by 42 days post-transplant, and 81% of them achieved neutrophil engraftment by Day 16 post-transplant, significantly more than the unmanipulated CBU group.

The study secondary endpoints supported the clinical benefit derived from the more rapid neutrophil engraftment. The following endpoints met statistical significance based on the multiple comparison adjustments:

- Platelet engraftment by 42 days post-transplant
- Grade 2/3 bacterial or invasive fungal infections by 100 days post-transplant
- Days alive and OOH in the first 100 days post-transplant

The percentage of patients achieving platelet engraftment was significantly higher in the omidubicel arm, with 55% of patients engrafted by Day 42 post-transplant. Among all platelet engrafters (PEP population), the median time to platelet engraftment in patients treated with omidubicel was 8 days faster than patients treated with unmanipulated CBU. Bacterial, fungal, and viral infection rates were lower in patients receiving omidubicel treatment at Days 100, 180 and 365. Specifically, 39% of patients in the omidubicel arm had a Grade 2-3 bacterial infection or invasive fungal infection within 100 days following transplant compared to 60% of patients randomized to unmanipulated CBU. This difference in favor of omidubicel was also seen at Day 180 and Day 365 post-transplant. Moreover, only 8% of patients randomized to omidubicel had a Grade 3 viral infection within 1-year following transplant compared to 27% of patients randomized to unmanipulated CBU. In the first 100 days following transplant, patients receiving omidubicel had a 12.5 days longer median duration alive and out of hospital.

A tertiary study endpoint assessed the impact of the rapid hematopoietic recovery and the decrease in infection risk on the mortality associated with transplant complications. NRM by 210 days post-randomization in patients randomized to omidubicel was 11% (7 deaths), compared to 24% (15 deaths) in patients randomized to unmanipulated CBU, demonstrating a consistent trend of reduction in the 210 days post-randomization NRM percentage of 13% ($p=0.086$). At 15 Months after randomization, the reduction in cumulative incidence of NRM for the omidubicel arm was 14% (from 29% to 15%) ($p=0.068$).

The study exploratory endpoints also assessed survival in the ITT population. Overall survival was observed to consistently favor the active arm over time. At 210 days post-randomization, there was a 16% increase in survival (68%-84%) for omidubicel patients with a 95% CI of 1% - 30% (p=0.04). At 15 Months post-randomization, there was a 12% increase in survival (60%-73%) for omidubicel patients with a 95% CI of –5%-28% (p=0.13).

While the study sample size limited the interpretation of patient subgroups, the main study outcomes were generally maintained across different demographic, disease, and prognostic subgroups, reflecting a comprehensive treatment effect.

12 SAFETY EVALUATION(S)

12.1 Extent of Exposure

A by-subject list of study drug administration is provided in Listing 16.2.5.1. Of 125 randomized patients, 52 patients received an omidubicel product within study specifications, three patients received an OOS omidubicel product per permission from FDA, and one patient (GP3KMC-004) received omidubicel off-study (this patient was not transplanted within 90 days of randomization). Fifty-six patients received an unmanipulated CBU transplant that met protocol criteria, and six patients received an unmanipulated CBU transplant that did not meet protocol criteria. The SP comprised all patients who received omidubicel on study and within specifications (n=52) and all unmanipulated CBU patients who received an unmanipulated CBU that met protocol criteria (n=56). The SP is identical to the AT population. Narratives for the 17 patients not included in the SP are provided in Section 14.3.1:

- GP3CCF-003
- GP3CCF-004
- GP3CCF-005
- GP3DFC-006
- GP3DFC-007
- GP3DUK-002
- GP3KMC-002
- GP3KMC-004
- GP3LAF-002
- GP3LAF-008
- GP3NWU-002
- GP3OHS-005
- GP3OHS-006
- GP3RCI-001
- GP3RMH-001
- GP3UMN-008
- GP3UMN-009

12.2 Adverse Events

12.2.1 Brief Summary of Adverse Events

Collection and reporting of AEs by study period is described in Section 9.5.2. Safety events are reported as of the cutoff date for the data analysis (April 29, 2021). Since omidubicel is a single use treatment, the safety evaluation described in this report focuses primarily on AEs that were treatment-emergent.

Study periods relevant to collection of AEs included the conditioning period, the immediate post-transplant period, near-term safety reporting, and longer-term safety reporting.

Safety reporting of anticipated events during conditioning sets a baseline patient status for AEs that can be compared to post-transplant status to determine if an adverse event is treatment-emergent or pre-existing due to the myeloablative conditioning regimen.

The immediate post-transplant period encompasses the start of the transplant infusion up through 24 hours after the end of the transplant infusion. Any event occurring or worsening during this time is defined as an infusion reaction, regardless of whether the transplant product was determined to cause the event. This broad definition was intended to ensure that potential safety signals immediately following the infusion were not missed. Many events related to the myeloablative therapy and unrelated to the transplant graft may start during this period. If an event did not increase in severity from what was originally reported during conditioning, it was

not included as a treatment-emergent adverse event (TEAE) unless the event resolved to a lower severity during or post-transplant and then increased to the original severity.

Near-term safety reporting encompassed the time period from Day 1 following transplant through Day 42 and captured the period of time when engraftment was occurring, the patient was still severely immunocompromised, and the adverse effects of conditioning, immunosuppression, and concomitant medications were still occurring. AEs were expected to occur at a very high frequency during this period and therefore data reporting of expected events was streamlined to allow for efficient data entry without risking missed safety signals. As described in Section 9.5.2, weekly reporting of the highest Grade of anticipated AEs was expected during this period, along with weekly grading of GvHD, and individual reporting of SAEs, infections, and unanticipated AEs.

Longer-term safety reporting encompassed Day 43 through the end of study. During this period, Grade 3-5 AEs, infections, and all SAEs were reported individually and GvHD was graded at every study visit. Grade 1-2 non-SAEs were not reported during this period. An overview of TEAEs by treatment group for the SP is provided in Table 31. At least one TEAE was reported in every patient, and a Grade 3-5 AE was reported in nearly all patients (98% of omidubicel [n=51] and 95% of unmanipulated CBU patients [n=52]). Treatment-emergent SAEs were reported in 90% (n=47) of omidubicel patients and 91% (n=51) of unmanipulated CBU patients. There were 21 related treatment-emergent SAEs in patients who received omidubicel versus 23 related treatment-emergent SAEs in patients who received unmanipulated CBU. Overall, 46% (n=24) and 52% (n=29) of patients had a TEAE related to omidubicel or unmanipulated CBU, respectively. In addition, 23% (n=12) of omidubicel patients had a treatment-emergent death whereas 36% (n=20) of unmanipulated CBU patients had a treatment-emergent death.

Table 31: Overview of Treatment-Emergent Adverse Events (Population: Safety Population)

	Treatment Received			
	Omidubicel		UCBU	
	Patients (N)	%	Patients (N)	%
Total number of patients in safety population	52	100.0	56	100.0
Patients with any treatment-emergent adverse event	52	100.0	56	100.0
Patients with any treatment-emergent adverse event possibly related to infused stem cell product	24	46.2	29	51.8
Patients with any treatment-emergent serious adverse event	47	90.4	51	91.1
Patients with any treatment-emergent serious adverse event possibly related to infused stem cell product	21	40.4	23	41.1
Patients with any treatment-emergent adverse event of Grade 3-4	51	98.1	52	92.9
Patients with any treatment-emergent adverse event of Grade 3-5	51	98.1	53	94.6
Patients with any treatment-emergent adverse event of Grade 4-5	19	36.5	30	53.6
Patients with any treatment-emergent adverse event of Grade 5	12	23.1	20	35.7

Data Source: Listing 16.2.7.11

Abbreviations: UCBU: Unmanipulated cord blood unit

12.2.2 Display of Adverse Events

A summary display of AEs for all patients is provided in Table 14.3.6.1 and Table 14.3.6.2. Listing 16.2.7.8 provides details of all AEs by patient.

12.2.3 Analysis of Adverse Events

12.2.3.1 Complications Following Myeloablative HSCT

Allogeneic HSCT following myeloablative conditioning, used to treat patients with life-threatening acute leukemias and lymphomas, is known to be associated with significant morbidity following transplantation. These complications are attributable to the underlying hematologic malignancy, effects of prior combination chemotherapy, the organ toxicities of the chemotherapy and radiotherapy utilized for myeloablative conditioning with resultant cytopenias, infusion of the graft, the immune-related effects of the allogeneic graft cells on the recipient, as well as secondary effects of concomitant medications used for prevention or treatment of these effects. From a systematic perspective, these AEs include infectious (viral, bacterial, fungal), immune (engraftment syndrome, GvHD), hematopoietic (neutropenia, thrombocytopenia, anemia), gastrointestinal (nausea, vomiting, mucositis), vascular (hepatic veno-occlusive disease, diffuse alveolar hemorrhage), malignant (post-transplant lymphoproliferative disease) and other sequelae (Apperley 2012).

In the first days following transplant, the toxicity of the conditioning regimen frequently leads to nausea, vomiting and painful mucositis. These may be followed by early complications including hemorrhagic cystitis, hepatic veno-occlusive disease, capillary leak syndrome, engraftment syndrome, diffuse alveolar hemorrhage, thrombotic microangiopathy, idiopathic pneumonia syndrome, and multiple organ dysfunction syndrome. Apart from these direct toxic effects of the chemotherapy and/or radiotherapy regimens, the myeloablation itself exerts a profound cytopenia, disrupting all normal hematopoietic and immune functions for a period that extends weeks to months after transplantation, with an associated risk of severe or life-threatening infections, as well as bleeding events. Early infections during the pre-engraftment phase include bacterial and fungal pathogens, while viral infections are usually observed later in the post-engraftment period. During the late post-transplant phase (> 100 days), allogeneic HSCT recipients are at risk for CMV, and other latent viruses, community-acquired respiratory viruses, and encapsulated bacterial infections. Late effects include secondary malignancies, such as post-transplant lymphoproliferative disorders and solid tumors, as well as multiple non-malignant chronic ocular, cardiac, respiratory, hepatic, renal, neurologic, vascular and hormonal dysfunctions.

AEs related to the graft cells include the immediate risks of allergic reactions or anaphylaxis around infusion, the risk of engraftment failure or graft rejection, the multi-organ effects of acute and chronic GvHD, development of malignancies of donor origin, transmission of serious infections, and transmission of rare genetic diseases. Supportive immunosuppressive or antimicrobial therapies administered to prevent or treat such complications further increase the risks of adverse drug effects.

The above events were specifically noted in the safety assessment of HPC, Cord Blood (FDA 2013). Primary graft failure was reported in 16% of patients, Grade II-IV acute GvHD was reported in 42% of patients, and Grade III-IV acute GvHD was reported in 19% of patients.

12.2.3.2 Toxicities Following Other Cell Therapy Products

Tisagenlecleucel and axicabtagene ciloleucel are cell therapy products used for the treatment of hematologic malignancies (FDA 2020, FDA 2021). Common adverse reactions (incidence greater than 20%) associated with tisagenlecleucel and/or axicabtagene ciloleucel are cytokine release syndrome, hypogammaglobulinemia, infections-pathogen unspecified, pyrexia, decreased appetite, headache, encephalopathy, hypotension, bleeding episodes, tachycardia, nausea, diarrhea, vomiting, viral infectious disorders, hypoxia, fatigue, acute kidney injury, edema, cough and delirium. Warnings and precautions were noted for hypersensitivity reactions, serious infections, prolonged cytopenias, hypogammaglobulinemia, and secondary malignancies.

12.2.3.3 Pre-Transplant Adverse Events

An assessment of AEs and other clinically significant events occurring prior to transplantation was performed. As described in Section 10.1, the duration between randomization and transplantation was longer in the omidubicel arm (42 vs. 26 days) due to the longer duration required for omidubicel manufacturing (Table 14.1.17.2).

Four patients on each arm relapsed during the period from randomization to transplant. Among these, two patients on the omidubicel arm and one patient on the unmanipulated CBU arm were subsequently re-treated to achieve disease remission and were able to proceed to transplantation within 90 days of randomization.

Prior to the start of conditioning, 12 patients randomized to receive omidubicel and ten patients randomized to receive unmanipulated CBU reported non-relapse SAEs. Among the 59 patients randomized to omidubicel who were transplanted, a total of 29 Grade 3-5 AEs were reported in 19 patients (32%) in the period post-randomization and prior to transplantation. This was comparable to 21 Grade 3-5 events reported in 19/58 transplanted patients (33%) randomized to the unmanipulated CBU arm.

Despite the longer interval between randomization and transplantation in patients transplanted with omidubicel, patient safety for the omidubicel arm did not appear to be compromised.

12.2.3.4 Grade 3-5 AEs During or Post-Transplant

Grade 3-5 TEAEs reported in at least 3% of either arm of the SP are summarized by treatment group, SOC, and PT (Table 32). Summaries of AEs reported in at least 3% of the SP and considered potentially related to study drug are presented in Section 12.2.3.5.

For patients treated with omidubicel, the most common Grade 3-5 AEs by PT were pain in 17 (33%) patients, mucosal inflammation in 16 (31%) patients, and hypertension in 13 (25%) patients. For patients treated with unmanipulated CBU, the most common Grade 3-5 AEs were hypertension in 21 (38%) patients, mucosal inflammation in 19 (34%) patients, gastrointestinal toxicity in 19 (34%) patients. Table 32 presents Grade 3-5 TEAEs by SOC and PT.

The rate of Grade 3-5 AEs was generally similar across the two treatment groups. As expected, given the results of the secondary and exploratory endpoint analyses of infections, serious infections were more common in patients transplanted with unmanipulated CBU. Asthenia, fevers, gastrointestinal, and respiratory events were all reported more frequently in patients treated with unmanipulated CBU. Pain was reported more frequently in the omidubicel group as discussed in Section 12.2.3.12.

AEs of specific interest are discussed in subsequent sections and include infusion reactions (12.2.3.8), graft failure (12.2.3.9), infections (12.2.3.10), GvHD (12.2.3.11), malignancies of donor origin (12.2.3.15), and potential class effect risks (12.2.3.16).

Table 32: Treatment-Emergent AEs with Severity Grades 3-5 Reported in at least 3% in either group of the Safety Population (SP)

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel (N=52)		UCBU (N=56)	
	Patients (n)	%	Patients (n)	%
Blood and lymphatic system disorders				
Febrile neutropenia	4	7.7	4	7.1
Thrombotic microangiopathy	1	1.9	3	5.4
Gastrointestinal disorders				
Diarrhea	1	1.9	3	5.4
Dysphagia	6	11.5	7	12.5
Gastrointestinal Hemorrhage	0	0.0	3	5.4
Gastrointestinal toxicity	10	19.2	19	33.9
Vomiting	3	5.8	2	3.6
General disorders and administration site conditions				
Asthenia	2	3.8	11	19.6
Mucosal inflammation	16	30.8	19	33.9
Multiple organ dysfunction syndrome	0	0.0	2	3.6
Edema	1	1.9	4	7.1
Pain	17	32.7	10	17.9
Pyrexia	1	1.9	6	10.7
Hepatobiliary disorders				
Veno-occlusive liver disease	2	3.8	4	7.1
Immune system disorders				
Acute graft-versus-host disease	4	7.7	1	1.8
Graft-versus-host disease	3	5.8	5	8.9
Graft-versus-host disease in gastrointestinal tract	5	9.6	6	10.7
Infections and infestations				
Cystitis	4	7.7	2	3.6
Cytomegalovirus viraemia	2	3.8	1	1.8
Herpes zoster	2	3.8	0	0.0
Human herpesvirus 6 infection	4	7.7	0	0.0
Pneumonia	4	7.7	5	8.9
Sepsis	3	5.8	1	1.8
Septic shock	1	1.9	8	14.3
Staphylococcal bacteremia	2	3.8	0	0.0
Injury, poisoning and procedural complications				

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel (N=52)		UCBU (N=56)	
	Patients (n)	%	Patients (n)	%
Femoral neck fracture	2	3.8	0	0.0
Transplant failure	3	5.8	5	8.9
Investigations				
Transaminases increased	4	7.7	1	1.8
Weight decreased	3	5.8	0	0.0
Metabolism and nutrition disorders				
Dehydration	3	5.8	2	3.6
Hyperglycemia	4	7.7	8	14.3
Hypoalbuminemia	1	1.9	3	5.4
Hypocalcemia	1	1.9	3	5.4
Hypokalemia	6	11.5	5	8.9
Hypomagnesemia	2	3.8	0	0.0
Hypophosphatemia	3	5.8	5	8.9
Musculoskeletal and connective tissue disorders				
Muscular weakness	1	1.9	2	3.6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Acute lymphocytic leukemia recurrent	3	5.8	0	0.0
Leukemia recurrent	4	7.7	5	8.9
Nervous system disorders				
Syncope	3	5.8	2	3.6
Psychiatric disorders				
Anxiety	1	1.9	3	5.4
Depression	0	0.0	2	3.6
Insomnia	1	1.9	2	3.6
Renal and urinary disorders				
Acute kidney injury	4	7.7	3	5.4
Cystitis hemorrhagic	0	0.0	2	3.6
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome	0	0.0	2	3.6
Acute respiratory failure	0	0.0	2	3.6
Dyspnea	4	7.7	9	16.1
Epistaxis	3	5.8	4	7.1
Hypoxia	5	9.6	13	23.2
Respiratory failure	2	3.8	5	8.9
Vascular disorders				
Hemorrhage	1	1.9	2	3.6
Hypertension	13	25.0	21	37.5

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel (N=52)		UCBU (N=56)	
	Patients (n)	%	Patients (n)	%
Hypotension	2	3.8	5	8.9

Data Source: Listing 16.2.7.11

N= Total number of patients in each treatment arm from the Safety Population; n= Number of patients with safety events by treatment arm

Abbreviations: UCBU: Unmanipulated cord blood unit.

12.2.3.5 Suspected Adverse Reactions

Suspected adverse reactions (defined as AEs suspected to be related to the infused study product) in at least 3% of the SP are summarized in Table 33. The most common suspected adverse reaction was GvHD, described in detail in Section 12.2.3.11. Other suspected AEs included hypertension (4% of omidubicel patients and 16% of unmanipulated CBU patients), graft failure (described in detail in Section 12.2.3.9), pain (6% of omidubicel patients and 2% of unmanipulated CBU patients), dyspnea (2% of omidubicel patients and 7% of unmanipulated CBU patients), hypoxia (2% of omidubicel patients and 4% of unmanipulated CBU patients) and thrombotic microangiopathy (4% of unmanipulated CBU patients). Pain and respiratory events are discussed in more detail in Sections 12.2.3.12 and 12.2.3.14, respectively.

Table 33: Treatment-Emergent AEs Related to Study Product Reported in at least 3% in either group of the Safety Population (SP)

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel (n=52)		UCBU (n=56)	
	Patients (n)	%	Patients (n)	%
Blood and lymphatic system disorders				
Thrombotic microangiopathy	0	0.0	2	3.6
General disorders and administration site conditions				
Pain	3	5.8	1	1.8
Immune system disorders				
Acute graft-versus-host disease	5	9.6	2	3.6
Graft-versus-host disease	4	7.7	5	8.9
Graft-versus-host disease in gastrointestinal tract	5	9.6	6	10.7
Graft-versus-host disease in skin	2	3.8	0	0.0
Injury, poisoning and procedural complications				
Transplant failure	2	3.8	5	8.9
Respiratory, thoracic and mediastinal disorders				
Dyspnea	1	1.9	4	7.1
Hypoxia	1	1.9	2	3.6
Vascular disorders				
Hypertension	2	3.8	9	16.1

Data Source: Listing 16.2.7.11

N= Total number of patients in each treatment arm from the Safety Population; n= Number of patients with safety events by treatment arm

Abbreviations: UCBU: Unmanipulated cord blood unit

12.2.3.6 Suspected Unexpected Adverse Reactions

Overall, seven AEs were reported as SUSARs related to omidubicel.

Clonal T-cell lymphocytosis was reported as a SUSAR in one patient treated with omidubicel (GP3CCF-002). Details are provided in Section 12.2.3.15.

Cord colitis was reported as a SUSAR in one patient treated with omidubicel (GP3DCH-002). The patient was a 17-year-old female with a primary diagnosis of AML. Two months after transplantation, the patient presented with diarrhea, vomiting and abdominal cramps. Infection and GvHD were ruled out, and the patient was diagnosed with cord colitis based on non-specific pathological findings. The patient improved with fluids and supportive care and was discharged.

Hyperacute Graft vs Host Disease (haGVHD) (MedDRA PT: Acute GvHD) was reported as a SUSAR in one patient treated with omidubicel (GP3CSA-001). The patient was a 20-year-old male with a primary diagnosis of ALL. Through two weeks following transplantation, the patient experienced increasing nausea, vomiting and diarrhea and was diagnosed with GvHD on skin biopsy following the appearance of a rash. The patient was treated with corticosteroids and defibrotide due to hepatosplenomegaly and suspicion of veno-occlusive disease/sinusoidal occlusive syndrome. Sirolimus and Etanercept were started due to lack of improvement, however respiratory failure developed, and the patient died 31 days post-transplantation due to progressive multiple organ failure and severe acute GvHD. Acute GvHD is an expected complication in HSCT, an event which is defined by several different PTs. The current case was the first in which the verbatim term hyperacute GvHD was specifically used as the reporting term.

Following request by the MHRA (UK competent authority), life-threatening and fatal suspected adverse reactions were not considered as expected and were considered a SUSAR for expedited reporting. Consequently, four cases of life-threatening or fatal acute GvHD (including the hyperacute GvHD event described above), and one case of graft failure were reported as SUSARs.

12.2.3.7 Serious Adverse Events

Nearly all patients on both treated groups experienced at least one treatment-emergent SAE. A total of 263 treatment-emergent SAEs were reported in 98 patients; 128 events in 47 patients treated with omidubicel and 135 events in 51 patients treated with unmanipulated CBU; a total of 16 pre-transplant SAEs were reported in 11 patients treated with omidubicel, and ten pre-transplant SAEs were reported in nine patients treated with unmanipulated CBU.

The percent of patients experiencing different types of SAEs are summarized by SOC and PT in Table 34. The most common SAE post-transplant was infection, experienced by 26 (50%) omidubicel patients and 28 (50%) unmanipulated CBU patients. The overall experience of infection is discussed in Section 12.2.3.10. GvHD was also a common SAE post-transplant and is discussed in detail in Section 12.2.3.11. Respiratory events were more commonly reported as SAEs in the unmanipulated CBU group, these events are discussed in Section 12.2.3.14. As per the Sponsor's request, relapse events were reported as SAEs, in order to enable a more complete description and assessment of the events.

Disease relapse is discussed in the efficacy evaluations in Section 11.4.5.

Renal disorders encompassing acute kidney injury, renal failure and renal impairment were reported as SAEs in seven omidubicel recipients, compared to two unmanipulated CBU recipients. The events in the omidubicel recipients were further assessed. Among these cases, renal disorders were assessed to be drug-induced in four patients and attributed to pre-renal hypovolemia or hypertension in two other patients. In two patients BK cystitis was also considered to be a contributing factor. The events resolved within several days with supportive care.

Table 34: Serious Adverse Event Reported in at least 3% in either group of the Safety Population (SP)

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel		UCBU	
	Number of Patients with Events	% of Patients	Number of Patients with Events	% of Patients
Blood and lymphatic system disorders	4	7.7	4	7.1
Febrile neutropenia	3	5.8	0	0.0
Thrombotic microangiopathy	1	1.9	4	7.1
Gastrointestinal disorders	6	11.5	13	23.2
Abdominal pain	1	1.9	2	3.6
Diarrhea	1	1.9	3	5.4
Gastrointestinal hemorrhage	0	0.0	2	3.6
General disorders and administration site conditions	6	11.5	6	10.7
Multiple organ dysfunction syndrome	0	0.0	2	3.6
Pyrexia	5	9.6	3	5.4
Hepatobiliary disorders	2	3.8	4	7.1
Veno-occlusive liver disease	2	3.8	4	7.1
Immune system disorders	17	32.7	14	25.0
Acute graft-versus-host disease	5	9.6	2	3.6
Graft-versus-host disease	4	7.7	5	8.9
Graft-versus-host disease in gastrointestinal tract	5	9.6	6	10.7
Graft-versus-host disease in skin	2	3.8	0	0.0
Infections and infestations	26	50.0	28	50.0
Bacteremia	0	0.0	2	3.6
Cytomegalovirus infection reactivation	2	3.8	1	1.8
Cytomegalovirus viraemia	2	3.8	1	1.8
Herpes zoster	2	3.8	0	0.0
Human herpesvirus 6 infection	4	7.7	1	1.8
Pneumonia	4	7.7	6	10.7
Sepsis	3	5.8	1	1.8
Septic shock	1	1.9	8	14.3
Staphylococcal bacteremia	2	3.8	0	0.0

Table 34: Serious Adverse Event Reported in at least 3% in either group of the Safety Population (SP)

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel		UCBU	
	Number of Patients with Events	% of Patients	Number of Patients with Events	% of Patients
Upper respiratory tract infection	0	0.0	2	3.6
Viral infection	2	3.8	0	0.0
Injury, poisoning and procedural complications	5	9.6	6	10.7
Femoral neck fracture	2	3.8	0	0.0
Transplant failure	3	5.8	5	8.9
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	8	15.4	6	10.7
Acute lymphocytic leukemia recurrent	3	5.8	0	0.0
Leukemia recurrent	4	7.7	6	10.7
Nervous system disorders	4	7.7	2	3.6
Subarachnoid hemorrhage	2	3.8	0	0.0
Renal and urinary disorders	7	13.5	5	8.9
Acute kidney injury	5	9.6	2	3.6
Cystitis hemorrhagic	0	0.0	3	5.4
Respiratory, thoracic and mediastinal disorders	8	15.4	15	26.8
Acute respiratory distress syndrome	0	0.0	2	3.6
Acute respiratory failure	0	0.0	2	3.6
Respiratory failure	2	3.8	5	8.9

Data Source: Listing 16.2.7.7

Abbreviations: UCBU: Unmanipulated cord blood unit

Serious Adverse Events (SAEs) related to the infused stem cell product are summarized in Table 35. GvHD was the most common related SAE and is described in detail in Section 12.2.3.11. Transplant failure (described in Section 12.2.3.9) was also a common related SAE. All other related SAEs occurred in a single patient.

Table 35: Percent of Patients with Related Serious Adverse Events by Preferred Term and System Organ Class (SP)

MedDRA Preferred Term by System Organ Class	Treatment Received			
	Omidubicel		UCBU	
	Number of Patients with Events	% of Patients	Number of Patients with Events	% of Patients
Blood and lymphatic system disorders				
Thrombotic microangiopathy	0	0.0	1	1.8
Congenital, familial and genetic disorders				
Acquired chromosomal abnormality	0	0.0	1	1.8
Gastrointestinal disorders				
Colitis	1	1.9	0	0.0
Gastrointestinal hemorrhage	0	0.0	1	1.8
Inflammatory bowel disease	0	0.0	1	1.8
Immune system disorders				
Acute graft-versus-host disease	5	9.6	2	3.6
Acute graft-versus-host disease in intestine	1	1.9	0	0.0
Chronic graft-versus-host disease	0	0.0	1	1.8
Graft-versus-host disease	4	7.7	5	8.9
Graft-versus-host disease in gastrointestinal tract	5	9.6	6	10.7
Graft-versus-host disease in skin	2	3.8	0	0.0
Injury, poisoning and procedural complications				
Infusion-related reaction	0	0.0	1	1.8
Transplant failure	2	3.8	5	8.9
Investigations				
T-lymphocyte count increased	1	1.9	0	0.0
Nervous system disorders				
Cerebral infarction	0	0.0	1	1.8
Respiratory, thoracic and mediastinal disorders				
Pulmonary alveolar hemorrhage	0	0.0	1	1.8

Data Source: Listing 16.2.7.7

Abbreviations: UCBU: Unmanipulated cord blood unit

12.2.3.8 Infusion Reactions

HSCT can be associated with serious, including fatal, infusion reactions (FDA 2013). Allergic reactions may occur with infusion, including serious hypersensitivity reactions such as anaphylaxis. Infusion reactions are also expected to occur, and severe reactions, including respiratory distress, severe bronchospasm, severe bradycardia with heart block or other arrhythmias, cardiac arrest, hypotension, hemolysis, elevated liver enzymes, renal compromise, encephalopathy, loss of consciousness, and seizure also may occur. In the COBLT study, 48% of infusions were associated with hypertension, and 21% were associated with Grade 3-4 hypertension. Other common infusion reactions were vomiting (15%), nausea (13%) and sinus bradycardia (10%) (FDA 2013).

Using a conservative approach, the protocol-defined infusion reaction as any AE that occurred or worsened between the start of omidubicel infusion and 24 hours after the end of omidubicel infusion. As such, all events in that time frame were designated as infusion reactions, regardless of whether they were deemed to be related to omidubicel or if they were a worsening of an existing condition.

Twenty-nine (56%) patients transplanted with omidubicel and 40 (71%) patients transplanted with unmanipulated CBU had at least one infusion reaction. This difference was evaluated using a Chi-square test (p=0.090). Of these, nine (17%) patients transplanted with omidubicel and 12 (21%) patients transplanted with unmanipulated CBU had a severe (CTCAE Grade 3-4) AE within 24 hours of infusion. Forty-three (83%) patients transplanted with omidubicel and 44 (79%) patients transplanted with unmanipulated CBU had only non-severe or no infusion reactions (Table 36).

Table 36: Adverse Event Summary for Infusion Reactions, Patient Level (SP)

	Treatment Received				
	Omidubicel		UCBU		
	N	%	N	%	*P*-Value
Patients with any infusion reactions	29	55.8	40	71.4	0.090
Patients with no infusion reactions	23	44.2	16	28.6	
Patients with severe infusion reactions	9	17.3	12	21.4	0.589

Data Source: Listing 16.2.7.3

N=Number of patients

Abbreviations: UCBU: Unmanipulated cord blood unit

The most common Grade 3 or 4 event was hypertension, reported in three (6%) patients treated with omidubicel and nine (16%) patients treated with unmanipulated CBU. Grade 3-4 infusion reactions occurring in more than one omidubicel recipient were hypertension, mucosal inflammation and dysphagia. Two patients in the omidubicel arm had Grade 4 infusion reactions; in both cases, the events began prior to transplantation (dyspnea in the setting of sepsis; mucosal inflammation in the setting of mucositis), however they worsened during the 24 hours following infusion and were therefore considered infusion reactions (Listing 16.2.7.3).

Overall, transplantation with omidubicel was not associated with an increase in the rate or severity of infusion reactions.

12.2.3.9 Graft Failure

Primary graft failure was defined as failure to achieve neutrophil engraftment by Day 42. Infusion of a second stem cell product on or prior to Day 42 was considered primary graft failure, with the following exception: infusion of an additional stem cell product after documented neutrophil engraftment was considered secondary graft failure, even if it occurred on or prior to Day 42.

Secondary graft failure was defined as documented neutrophil engraftment, followed by severe neutropenia (<0.5 x 10^9/L for three or more consecutive laboratory values on separate days) with marrow cellularity <5%, without subsequent improvement occurring either spontaneously or after growth factor treatment. Infusion of an additional stem cell product after documented neutrophil engraftment was considered secondary graft failure.

Graft failure is an indication of failure of the transplant procedure and was therefore also analyzed in the efficacy endpoints for omidubicel. Graft failure following myeloablative conditioning may be fatal, as recovery of the host hematopoietic system is unlikely. Secondary graft failure is a known complication following HSCT (Rondon, Saliba et al. 2008). Multiple factors can contribute to secondary graft failure, including graft rejection, viral infection, GvHD, medications, or persistent disease.

Primary engraftment failure not due to competing risks was assessed in the ITT population as well as in the SP. In the SP, primary engraftment failure occurred in 2% of patients treated with omidubicel, compared to 9% of patients treated with unmanipulated CBU (Table 14.2.15.3.1). The difference in proportion with engraftment failure was 7% (95% CI –1% - 16%; p=0.21).

Among the omidubicel patients in the SP, two patients failed to engraft. One additional patient who received an OOS omidubicel product (GP3NWU-002) also failed to engraft. Among the unmanipulated CBU patients in the SP, five patients failed to engraft. One additional patient received an unmanipulated back-up CBU that did not meet the protocol requirements, due to omidubicel production failure (GP3RMH-001). This patient also failed to engraft.

Table 37 outlines details on these patients' baseline, transplant characteristics and post-transplant main events.

Table 37: Omidubicel Patients who Failed to Engraft

Patient ID	Demographics	Disease Characteristics	Conditioning	Transplanted Product	Post-transplant events	Events Resolution
GP3NWU-002	Asian male / 32 yo	AML moderate risk	Thiotepa, Busulfan, Fludarabine	OOS omidubicel infused under FDA approval. Omidubicel CF: -TNC: 0.65×10^9 cells (minimal specification: 0.8×10^9 cells) - CD34+: 1×10^8 cells (1.3×10^6 CD34+ cells/kg)	- Primary graft failure (pre and post-transplant complicated with C. Difficile infection treated with vancomycine, BK viruria and HHV6 viremia treated with foscarnet) - Second transplant from haploidentical donor after 36 days, with subsequent engraftment, in parallel with sepsis event - Secondary graft failure - Received two additional haploidentical CD34+ cell infusions with intercurrent infectious episodes - Relapse on Day 134 following initial transplantation	Patient died from multi-organ failure at 180 days following initial transplantation
GP3DUK-021	White female / 58 yo	MDS	TBI, Fludarabine, Thiotepa	Omidubicel numerically below required specifications (FDA approve this patient to be considered infused as within specifications) Omidubicel NF: TNC 3.9×10^8 cells (minimal specification is 0.4×10^9 cells) NF infused in 8 minutes, shorter than the 10 minutes minimal duration of infusion indicated on the CoA; Sponsor assessment indicated no resulting safety concern (actual	- Neutrophil recovery by 12 days - post-transplant subsequent chimerism (14 days post-transplant) showed 82% donor chimerism (full donor chimerism defined as $\geq$ 90% donor cells) - Later chimerism showed increasing host chimerism in parallel to diagnosis of disease progression	Patient died from relapse 241 days following transplantation despite re-treatment

Patient ID	Demographics	Disease Characteristics	Conditioning	Transplanted Product	Post-transplant events	Events Resolution
				calculated minimal infusion time was two minutes)		
GP3LAF-011	Female / 36 yo (race/ethnicity unknown/not reported)	AML	Thiotepa, Busulfan, Fludarabine	- Omidubicel within specifications - Infusion solution used for dilution of CF and NF was held at a temperature of 9.8°C (higher than the allowed maximal 8°C) for 1:11 hours. Sponsor subsequent assessment indicated no safety implications since the infusion solution is stable for 30 hours in room temperature.	- Post-transplant HHV6 infection (Day 21: 4690 copies/mL; Day 28: 43024 copies/mL); no treatment provided. - Methylprednisolone given on days 26-28 for suspected skin GvHD (rash) but no suspicion of engraftment syndrome noted. - No neutrophil recovery demonstrated. - Patient received a second transplant from a haploidentical donor 40 days following the initial transplantation, with subsequent engraftment.	Patient alive at 15 Months post initial transplant

Data Source: Patient narratives GP3NWU-002, GP3DUK-021, GP3LAF-011

Abbreviations: AML: Acute myelogenous leukemia; CF: Cultured fraction; CoA: Certificate of analysis; GvHD: Graft versus host disease; HHV-6: Human herpesvirus 6; MDS: Myelodysplastic syndrome; NF: Non-cultured fraction; OOS: Out of specification; TBI: Total body irradiation; TNC: Total nucleated cells; yo: Years old

One patient treated with omidubicel had a secondary graft failure approximately six months following transplantation, concurrent with a diagnosis of ALL relapse. This patient (GP3DUK-015) was an 18-year-old Black female with a primary diagnosis of ALL, moderate risk. The patient was transplanted with omidubicel and engrafted neutrophils eight days post-transplant, and neutrophils 25 days post-transplant. The post-transplant recovery was notable for obesity, Grade II acute GvHD, and hyperglycemia. The patient presented 202 days following transplant with pancytopenia and secondary graft failure concomitant with disease relapse were diagnosed. The patient received a second transplantation from a haploidentical donor and engraftment was reported.

No cases of secondary graft failure were reported in patients treated with unmanipulated CBU.

Graft failure is a severe risk of HSCT, however the limited number of events among omidubicel recipients did not indicate a particular safety risk beyond the known experience in myeloablative HSCT.

12.2.3.10 Infections

Infections of all types are common complications in the setting of HSCT, due to the myeloablation and other therapies resulting in substantial immunosuppression. Infection is closely linked with the kinetics of hematopoietic recovery and immune reconstitution and was therefore also discussed as an efficacy endpoint. During the pre-engraftment phase, 0 to 30 days following transplant, the most prevalent pathogens causing infection are bacteria and Candida species and, if the neutropenia persists, Aspergillus species (Afessa and Peters 2006). Sauter et al. reported that bacterial infections and fungal infections affected 32% and 14% of patients, respectively, within the first 30 days (Sauter, Abboud et al. 2011). The early post-engraftment phase (30 to 100 days) is characterized by cytomegalovirus (CMV), adenovirus and others, Pneumocystis jiroveci, and Aspergillus infections. During the late post-transplant phase (> 100 days), allogeneic HSCT recipients are at risk for CMV, and other latent viruses, community-acquired respiratory viruses, and encapsulated bacterial infections. Viral infections generally have the highest lethality (Sauter, Abboud et al. 2011).

In this study, pre-existing uncontrolled infections were a contraindication to transplant, and strict guidelines for hygiene and care were applied to patients on study. The study mandated or recommended prophylactic medications for viral, bacterial, and fungal infections and PCP. The protocol also specified surveillance testing for CMV, EBV, and HHV6, as well as procedures for identifying bacterial pathogens in patients with suspected infections. Treatment of infections was generally expected to follow standard institutional guidelines, with an aggressive approach appropriate to the HSCT setting.

Infections were analyzed as part of the study secondary and exploratory endpoints. As described in Section 11.4.3, patients in the omidubicel group had a lower risk of experiencing a Grade 2/3 (moderate – severe) bacterial or invasive fungal infection by 100 days following transplantation as well as a lower risk of a Grade 3 (severe) viral infection within a year post-transplant compared to the unmanipulated CBU group.

Overall Infection Experience

Table 14.3.9.1 shows the highest Grade of bacterial, viral, and fungal infections experienced by patients in each arm.

Sixty-five percent of omidubicel patients experienced at least one bacterial infection of any Grade compared to 80% of patients in the unmanipulated CBU group. Bacterial infections were more severe in the unmanipulated CBU arm; 70% of unmanipulated CBU patients experienced at least one Grade 2-3 infection compared to 35% of omidubicel patients.

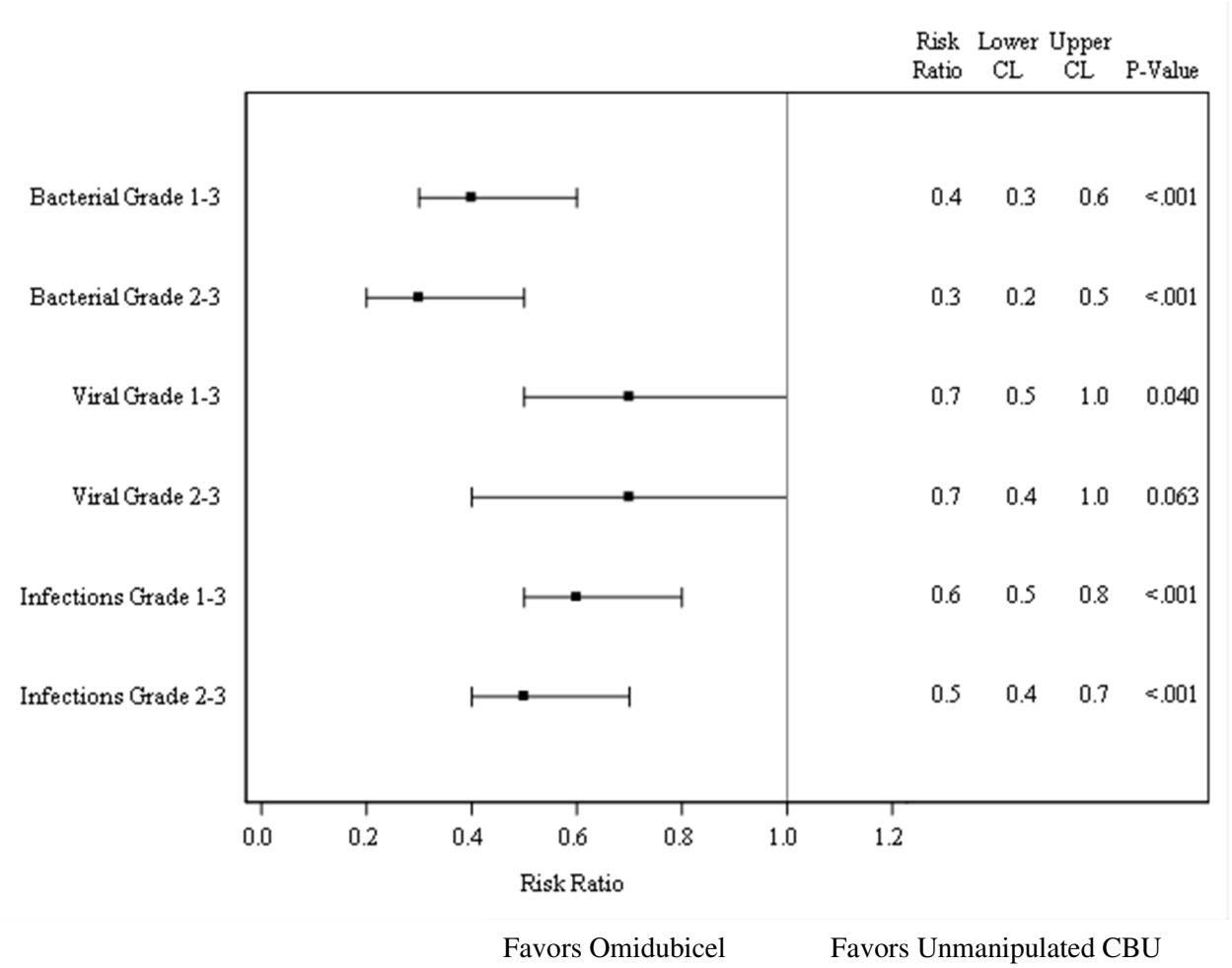
The overall experience of viral infections was more similar between treatment groups. Seventy-five- percent of omidubicel patients experienced at least one viral infection of any Grade compared to 80% in the unmanipulated CBU group. However, similar to the experience with bacterial infections, viral infections tended to be more severe in the unmanipulated CBU group compared to the omidubicel group. In the unmanipulated CBU group 27% of patients experienced a Grade 3 viral infection compared to 8% in the omidubicel group.

Fungal infections were less frequent and overall similar between groups; 21% of omidubicel patients compared to 27% of unmanipulated CBU patients with at least one fungal infection of any Grade. However only 6% of omidubicel patients had a Grade 3 fungal infection, compared to 18% of unmanipulated CBU patients.

Non-microbiologically defined infections were also similar between groups; 35% of omidubicel patients compared to 25% of unmanipulated CBU patients. Severe non-microbiologically defined infections were also similar; 29% of omidubicel patients versus 20% of unmanipulated CBU patients with at least one Grade 2 or 3 non-microbiologically defined infection.

To account for the possibility of multiple infections per patient and relative differences in periods of risk between the treatment groups, a post hoc analysis of infection “density,” defined as the total number of infections per patient adjusted for total follow-up time, during the first year following transplantation was performed. Infection densities were compared using the generalized estimating equation approach for a linear model with two periods (0-30 and 31-365 days post-transplant) and a negative binomial link. The risk ratio for total infections (defined as the rate of infection in omidubicel patients relative to the rate of infection in standard cord patients), irrespective of severity, was significantly lower among recipients of omidubicel compared to unmanipulated CBU. The same observation was made when bacterial or viral infections were analyzed individually (Figure 24).

Figure 24: Infection Density Following Transplantation (AT Population)



Data Source: Listing 16.2.7.9

Note: The Infections category noted above includes all infections (e.g. bacterial, viral, fungal, protozoal, and non-microbiologically defined).

Estimates are from the treatment effect (omidubicel vs. unmanipulated CBU) parameter in a GEE with a categorical grouping of time (Day 0-30, Day 31-365 post-transplant), a negative binomial distribution, and an offset for log (days at risk). The confidence limits are asymptotic 95% confidence intervals.

The number of patients in each group that reported a suspected infection that was treated but not confirmed was also explored (Table 14.3.9.2, Table 14.3.9.3). In the SP population, the number of suspected infections was similar between the groups; 75% of omidubicel patients (93 total suspected infections) compared to 70% of unmanipulated CBU patients (97 total suspected infections).

As discussed in the efficacy summary, the overall infections experience appeared to demonstrate a safer and more beneficial profile for omidubicel recipients.

12.2.3.11 GvHD

Acute and chronic GvHD are multi-system disorders that are common and potentially severe complications of allogeneic HSCT. GvHD occurs when immune cells from a donor graft recognize the transplant recipient host as foreign and initiate an immune reaction. Acute GvHD

usually presents around the time of engraftment and manifests as maculopapular rash, nausea, vomiting, abdominal pain, diarrhea, or increased serum bilirubin. Chronic GvHD is usually diagnosed later throughout the first year post-transplant. Clinical manifestations include a scleroderma-like or lichen planus- like skin involvement, gastrointestinal ulcerations and sclerosis of the gastrointestinal (GI) tract, and increased bilirubin.

GvHD was reported on separate GvHD forms, to assess and quantify the degree of involvement of the skin, liver, and gastrointestinal tract. Acute GvHD was graded as Grade I-IV using the Consensus Conference on Acute GvHD grading (Przepiorka, Weisdorf et al. 1995). Chronic GvHD was graded according to the NIH Consensus Criteria (Filipovich, Weisdorf et al. 2005, Jagasia, Greinix et al. 2015).

Acute and chronic GvHD were analyzed in the TP population, which included all patients who received omidubicel or unmanipulated CBT within 90 days post-randomization. Patients were analyzed according to the treatment groups to which they were allocated, regardless of whether they received the assigned graft per protocol. Overall, the TP population comprised 59 patients in the omidubicel group and 58 patients in the unmanipulated CBU group.

The primary analyses of acute and chronic GvHD were based on the cause-specific HR obtained from a Cox regression analysis. This analysis was designed to consider potentially higher survival rates in the omidubicel arm, rendering a greater proportion of patients exposed to risk of GvHD. The secondary analyses were based on the cumulative incidence curves, with death, relapse, failure to achieve neutrophil engraftment, secondary graft failure and second SCT considered competing events.

Overall, no statistically significant differences were found in the experience of GvHD between groups.

Acute GvHD

Acute GvHD, was analyzed through 100 days following transplantation on the TP population. In the omidubicel group 24 (41%) patients had Grade II, seven (12%) patients had Grade III, and one (2%) patient had Grade IV acute GvHD as the maximum severity of acute GvHD experienced in the first 100 days. In the unmanipulated CBU group, 13 (22%) patients had Grade II, 12 (21%) patients had Grade III, and zero patients had Grade IV acute GvHD as the maximum severity of acute GvHD experienced in the first 100 days. While the rate of Grade II-IV acute GvHD was slightly higher in the omidubicel group than in the unmanipulated CBU group, the rates of Grade III-IV GvHD were similar. As shown in Figure 14.2.16.2.1, the cumulative incidence of Grade II-IV acute GvHD was 56% in the omidubicel group and 43% in the unmanipulated CBU group. Table 14.2.16.1.1 shows the Cox regression analysis of Grade II-IV GvHD, demonstrating a cause-specific HR of Grade II-IV GvHD with omidubicel of 1.48 (95% CI: 0.87 - 2.49, p=0.14). Conversely, the cumulative incidence of more serious Grade III-IV acute GvHD was 14% in the omidubicel group and 21% in the unmanipulated CBU group (Table 14.2.17.2.1), and as presented in Table 14.2.17.1.1, the HR for Grade III-IV GvHD with omidubicel was 0.65 (95% CI: 0.23 - 1.60, p=0.35).

Post hoc analyses of GvHD were performed on the SP, demonstrating similar results. The cumulative incidence of Grade II-IV acute GvHD was 60% in the omidubicel group and 43% in the unmanipulated CBU group (p=0.08) (Table 14.2.16.3.2). The cumulative incidence of

Grade III-IV acute GvHD was 15% in the omidubicel group and 20% in the unmanipulated CBU group (Table 14.2.17.3.2).

Chronic GvHD

Chronic GvHD was analyzed at 180 days and 1 year following transplantation in the TP population.

The incidence of chronic GvHD was similar in the two treatment groups. At 180 days, there were five cases of chronic GvHD in the omidubicel group and six cases in the unmanipulated CBU group. The cumulative incidence of chronic GvHD was 9% in the omidubicel group and 11% in the unmanipulated CBU group as shown in Table 14.2.18.2.1. The cause-specific HR was 0.80 (95% CI: 0.16 – 3.16, p=0.72) (Table 14.2.18.1.1).

In the omidubicel TP group, six (10%) patients had mild, ten (17%) patients had moderate and two (3%) patients had severe chronic GvHD as the maximum severity of chronic GvHD through 1-year post-transplant (Table 14.2.18.1.2). In the unmanipulated CBU group, three (5%) patients had mild, ten (17%) patients had moderate and two (3%) patients had severe chronic GvHD as the maximum severity of chronic GvHD through 1-year post-transplant (Table 14.2.18.1.2). At one year, the cumulative incidence was 34% in the omidubicel group and 29% in the unmanipulated CBU group, as presented in Table 14.2.19.2.1 and in Figure 14.2.19.2.1, and the HR was 1.06 (95% CI: 0.52 – 2.21, p=0.87) (Table 14.2.19.1.1). The one year cumulative incidence of moderate to severe chronic GvHD was 23% in both groups (Table 14.2.27.1).

Post hoc analyses of GvHD were performed on the SP, demonstrating similar results (Table 14.2.19.3.2). The cumulative incidence of chronic GvHD at one year was 38% for omidubicel recipients and 27% for unmanipulated CBU recipients.

GvHD was noted as the primary cause of death for six patients on the study. Of these patients, three patients were treated with omidubicel and three were treated with unmanipulated CBU. See Table 14.3.8.2 for details. In addition, GvHD was noted among secondary causes of death for one patient treated with omidubicel and three patients treated with unmanipulated CBU.

Acute GvHD can manifest in the skin, the liver or the upper or lower gastrointestinal tract. While hepatic or gastrointestinal involvement may progress to substantial organ dysfunction and potential residual chronic sequelae, skin involvement is generally more therapeutically manageable and associated with less severe sequelae (Castilla-Llorente, Martin et al. 2014). A review of the organs involved in acute GvHD events demonstrated a similar rate of hepatic and gastrointestinal organ involvement, however a numerically higher frequency of acute GvHD events involving the skin in the omidubicel group. For a comprehensive overview, acute GvHD was assessed through 180 days post-transplant. Twenty-three omidubicel patients had skin involvement compared to 14 unmanipulated CBU patients. Thus, it appears that the numerically higher number of acute GvHD cases in the omidubicel group is primarily due to a higher number of skin-related acute GvHD events.

In terms of chronic GvHD, 18 omidubicel patients and 15 unmanipulated CBU patients reported any Grade chronic GvHD. Among these patients, involvement of the skin, oral or genital mucosae was reported in 15 omidubicel patients and 11 unmanipulated CBU patients and was mild or moderate in severity aside from two severe cases reported in each group.

Overall, rates of acute and chronic GvHD were similar across the two arms, suggesting that omidubicel maintained the favorable GvHD profile associated with CBT compared with other HSCT graft modalities, allowing the successful utility of partially HLA-matched grafts for allogeneic HSCT, with an acceptable rate of GvHD.

Table 38: Deaths Due to GvHD

Treatment Assigned/Received	Patient ID	Age (Yrs)	Gender	Disease	Primary Cause of Death	Secondary Causes of Death	Days Post Transplant
Omidubicel	GP3CSA-001	19	Male	ALL	GvHD, acute		31
Omidubicel	GP3DUK-016	51	Female	Lymphoma	GvHD, acute	Organ failure, pulmonary; Organ failure, liver; Organ failure, cardiac	92
Omidubicel	GP3DUK-018	50	Male	AML	GvHD, acute	Infection, viral	61
UCBU	GP3KMC-001	18	Male	ALL	GvHD, acute		58
UCBU	GP3KMC-003	35	Male	AML	GvHD, chronic		151
UCBU	GP3LAF-005	20	Male	AML	GvHD, acute	Organ failure, pulmonary	135

Data Source: Listing 16.2.7.1

Abbreviations: ALL: Acute lymphoblastic leukemia, AML: Acute myelogenous leukemia; GvHD: Graft versus host disease; UCBU: Unmanipulated cord blood unit; Yrs: Years

Subgroups

The omidubicel SP patients were further assessed for any specific subgroups demonstrating a higher frequency or severity of acute GvHD, including patient gender, age, race/ethnicity, disease, disease risk, comorbidities, and geographical distribution.

Among patients transplanted with omidubicel, 32/52 patients reported Grade II-IV acute GvHD. In the control group, 24/56 patients reported Grade II-IV acute GvHD. The frequency of GvHD events was similar among different subgroups encompassing baseline patient or disease characteristics, considering the limited patient numbers in most of the subgroups.

The level of HLA mismatch between the donor and the recipient is a potential contributor to the development of GvHD and has also been implicated in the development of GvHD following CBT (Eapen, Klein et al. 2014). A review of HLA mismatch disparity among omidubicel recipients was performed (SP population). No differences were observed in the rate of acute GvHD when considering HLA mismatch at the antigen-level, indicating similar frequencies of acute GvHD in patients with a well matched 5/6-6/6 graft compared to a more mismatched 4/6 HLA-matched graft. Interestingly, when considering the HLA mismatch at the more stringent allelic level, it was demonstrated that among 16 omidubicel patients who had a 4/8 mismatched graft or lower, 12 (75%) patients developed Grade II-IV acute GvHD. Conversely, among patients who had a graft that was 5/8 HLA-matched or above, only 19/35 (54%) developed Grade II-IV acute GvHD. Among the patients who received unmanipulated CBU transplant and had a graft that was 5/8 HLA-matched or above, only 10/31 (32%) developed Grade II-IV acute GvHD.

Of note, among omidubicel patients treated with a TBI-based conditioning, 21/27 patients (78%) developed Grade II-IV acute GvHD, compared to 11/25 (44%) of the patients treated with a chemotherapy-based conditioning. A similar trend was not observed for the unmanipulated CBU group, with 11/28 (39%) of patients treated with a TBI-based conditioning developed Grade II-IV acute GvHD, compared to 13/28 (46%) of patients treated with chemo-based conditioning.

12.2.3.12 Pain and Mucositis

As noted in Table 32, the occurrence of Grade 3 pain in the SP was reported for 17 (33%) of omidubicel and 10 (18%) of unmanipulated CBU patients following transplantation.

The omidubicel recipients who reported pain post-transplant had similar baseline characteristics as the overall SP, with 47% male, and a median age 41 years (range 14 – 61 years). Similar to the overall SP experience, these patients engrafted at a median 11 days (range 7 – 25 days).

In order to further assess these events, the frequency of the reports of pain and their timing in relation to transplant were examined.

All the pain events were reported during the first 42 days post-transplant, in the context of the events known to commonly appear following transplant and reported as the maximal Grade over a period of time, rather than as individual events. The timing of reporting is detailed in Table 39. In this table, if pain persisted for an individual patient over multiple reporting intervals, that patient is counted in each applicable row.

Table 39: Timing of Grade 3 Pain Reported Following Transplantation (SP)

Reporting Interval	Omidubicel (Number of Patients Reporting Pain During the Time Period)	UCBU (Number of Patients Reporting Pain During the Time Period)
Transplant Day	0	1
By Day 7	8	5
By Day 14	4	4
By Day 21	3	1
By Day 28	2	2
By Day 35	6	2
By Day 42	5	0

Data Source: Listing 16.2.7.8

Abbreviations: UCBU: Unmanipulated cord blood unit

The reporting of such events was not accompanied with details of the etiology of pain, and therefore in order to assess these events more generally, the common causes of pain over the first weeks following transplant were considered: mucositis, acute GvHD, use of G-CSF, associated infections (cystitis, gastritis and typhlitis) and pre-existing pain (reported on the FACT-BMT) questionnaire at screening). Importantly, 25 of the 27 patients reported to have Grade 3 pain had at least one of the above potential underlying causes reported (one additional patient had a report of migraine concurrent to the reporting of pain, and one patient had an episode of severe abdominal pain requiring oxycodone to resolve).

Three omidubicel patients and one unmanipulated CBU patient had Grade 3 pain events that were reported to be related to the infused graft: pain reported concurrently with acute GvHD

(three omidubicel patients), and a cerebral infarction reported as an infusion-related SAE (one unmanipulated CBU patient).

Among the above listed potential etiologies for pain, the events of acute GvHD and infections were analyzed extensively and described separately in Section 12.2.3.11 and 12.2.3.10,respectively. An additional event that occurred frequently and is known to be associated with pain is mucositis, and therefore this event was analyzed separately, to assess for any differences among the two groups.

Oral mucositis is a major source of morbidity in patients undergoing HSCT (Sonis, Oster et al. 2001, Jones, Qazilbash et al. 2008). It is typically painful, impairs nutritional intake and requires intensive supportive care and hospitalization. Severe oral mucositis (Grades 3-4) is experienced by approximately two thirds of patients who undergo myeloablative conditioning for HSCT (Wardley, Jayson et al. 2000).

Mucositis was reported throughout Days -1 to 42 post-transplant as a maximal Grade across a period of time. By definition, Grade 2 or higher mucositis is associated with painful erythema, oedema or ulcers. Although not all mucositis cases on the study were concomitantly reported with pain, the overall frequency and severity of mucositis was assessed for a more comprehensive assessment.

Overall, mucositis was reported for 39 omidubicel patients and 47 unmanipulated CBU patients. Although Grade 1-2 mucositis events were reported together and could not be differentiated, Grade 4 mucositis was reported for one omidubicel patient, and Grade 3 mucositis was reported for 15 omidubicel patients and 19 unmanipulated CBU patients.

In summary, while the direct causes for pain were not reported, an assessment of the main possible etiologies of pain over the period they were reported did not indicate any potential safety risk beyond the known risks of myeloablative HSCT.

12.2.3.13 Hypertension

As noted in Table 32, a total of 13 (25%) omidubicel patients and 21 (37.5%) unmanipulated CBU patients reported a Grade 3 treatment-emergent hypertension event. No Grade 4 or 5 hypertension events were reported.

The omidubicel recipients who had hypertension post-transplant had similar baseline characteristics as the overall SP, with 54% male, and a median age 40 years (range 13 – 62 years). One omidubicel recipient, and 17-year-old female (GP3DCH-002) had an acute kidney injury 51 days post-transplant that was attributed to hypertension. The event was reported to have resolved within one day.

As hypertension is a frequent and potentially serious event occurring following transplant, this adverse event was further analyzed. Among patients treated with unmanipulated CBU, hypertension was reported to occur in 21% of transplant recipients (FDA 2013).

Grade 3 hypertension (systolic BP ≥160 mmHg or diastolic BP ≥100 mmHg) requires medical intervention with more than one drug. Among patients with Grade 3 hypertension events occurring through Day 42 post-transplant, three omidubicel patients and nine unmanipulated CBU patients had Grade 3 hypertension reported on the day of infusion, thus indicating that the observed difference between the arms is primarily attributable to differences in hypertension on Day 0. Among the events reported on Day 0, none of the events reported for omidubicel patients

were considered related to the infused graft, while seven unmanipulated CBU patients had hypertension events that were considered related to the graft. Of note, all these patients were transplanted with a double CBU transplant. A double unmanipulated CBU infusion is associated with a higher volume than omidubicel infusion (300-800 mL, depending on the preparation, compared to 150 mL for omidubicel), and furthermore unmanipulated CBUs may occasionally contain residual cellular debris, such as lysed RBCs, which are washed out of omidubicel during manufacturing. Such cellular debris may lead to transient renal dysfunction and hypertension.

Other contributing factors to hypertension on the day of transplant include the aggressive pre and post infusion hydration provided as supportive therapy.

Overall, hypertension is a known complication following HSCT, particularly in the setting of the graft infusion. The observed higher rate of hypertension for unmanipulated CBU recipients may be attributable to the infusion of two CBUs for transplant in many cases, as well as residual cellular debris remaining in the CBU.

12.2.3.14 Respiratory Events

As noted in Table 40, SAEs related to respiratory disorders were reported for eight omidubicel patients and 15 unmanipulated CBU patients.

Table 40 details the event terms for the two groups. As shown, each group had one event of pulmonary embolism, bronchospasm, and alveolar hemorrhage. This assessment focused on the occurrence of the following events in both groups (highlighted in bold in Table 40): respiratory failure, acute respiratory arrest syndrome, acute respiratory failure, hypoxia, idiopathic interstitial pneumonia, idiopathic pneumonia syndrome, and respiratory distress. Among these events, two patients in the omidubicel group had Grade 4 SAEs, involving life-threatening respiratory consequences requiring urgent intervention, intubation or ventilatory support, while in the unmanipulated CBU group six patients had Grade 5 fatal respiratory SAEs, five patients had Grade 4 SAEs, and one patient had a Grade 3 SAE.

Table 40: Names and Incidence of SAEs Related to Respiratory, Thoracic or Mediastinal Events

Omidubicel – 8 events in 8 patients	UCBU – 17 events in 15 patients
Pulmonary Embolism (1)	Pulmonary Embolism (1)
Bronchospasm (1)	Bronchospasm (1)
Alveolar Hemorrhage (1)	Alveolar Hemorrhage (1)
Respiratory Failure (2)	Acute Respiratory Arrest Syndrome (2)
Epistaxis (1)	Acute Respiratory Failure (2)
Laryngeal edema (1)	Hypoxia (1)
Pneumonia, aspiration (1)	Idiopathic Interstitial Pneumonia (1)
	Idiopathic Pneumonia Syndrome (1)
	Respiratory Distress (1)
	Respiratory Failure (5)
	Pleural Effusion (1)

Data Source: Listing 16.2.7.7

Abbreviations: UCBU: Unmanipulated cord blood unit

In the omidubicel group, two patients reported respiratory failure compared to 12 patients who reported respiratory failure or related events in the unmanipulated CBU group (Table 41).

Table 41: Respiratory Failure or Related Events in Safety Population (SP)

Treatment Group	Patient ID	Age (Yrs)	Gender	Diagnosis	AE	Grade	Additional Description
Omidubicel	GP3UTR-001	18	Female	AML	Respiratory insufficiency	4	AE Required ICU admission and intubation, thought to be an immune-mediated lung disease
	GP3DFC-001	47	Male	ALL	Hypoxic respiratory failure	4	AE in the setting of acute fluid overload and need for dialysis
UCBU	GP3CCF-007	44	Male	AML	IPS	5	
	GP3CHC-005	16	Male	ALL	Acute respiratory distress syndrome possibly associated with IPS	5	
	GP3DFC-003	23	Male	ALL	Idiopathic interstitial pneumonia	5	
	GP3SGH-001	22	Female	Biphenotypic Leukemia	Respiratory failure	5	AE thought to be related to TRALI and was treated with Tituxan
	GP3SGH-002	16	Female	CML	Respiratory failure	5	AE in the setting of pulmonary GvHD and Aspergillus infection
	GP3SGH-003	40	Female	AML	Respiratory failure	5	AE thought to possibly be related to hospital acquired pneumonia, fluid overload, and/or concurrent rhinovirus upper respiratory infection
	GP3CAL-003	32	Female	AML	Hypoxic respiratory failure	4	AE thought to be related to a mucus plug in the setting of sepsis and disseminated intravascular coagulation
	GP3KMC-001	18	Male	ALL	Acute respiratory failure	4	AE in the setting of severe GvHD
	GP3LOY-011	64	Male	AML	Respiratory distress	4	AE related to aspiration pneumonia following bacteremia
	GP3UTN-001	58	Male	MDS	Acute respiratory failure	4	AE though to be related to hyperacute GvHD
	GP3UTR-002	17	Female	ALL	ARDS	4	AE in the setting of lower respiratory adenovirus infection
					Respiratory insufficiency	3	AE in the setting of gram-negative sepsis

Treatment Group	Patient ID	Age (Yrs)	Gender	Diagnosis	AE	Grade	Additional Description
	GP3SCI-006	41	Male	Dendritic cell leukemia	Hypoxia	3	AE in the setting of GvHD and infection

Data Source: Listing 16.2.7.8

Abbreviations: AE: Adverse event; ALL: Acute lymphoblastic leukemia; AML: Acute myelogenous leukemia; ARDS: Acute respiratory distress syndrome; CML: Chronic myeloid leukemia; GvHD: Graft versus host disease; ICU: Intensive care unit; IPS: Idiopathic pneumonia syndrome; MDS: Myelodysplastic syndrome; TRALI: Transfusion-related acute lung injury; UCBU: Unmanipulated cord blood unit; Yrs: Years

Importantly, while the two respiratory events for the omidubicel patients were not related to any concurrent or recent infections, at least seven of the 13 events in the unmanipulated CBU group were related to recent or concurrent infections, as noted in Table 41. This observation may suggest that the lower frequency of infections for omidubicel treated patients could explain the lower frequency of respiratory failures and related severe pulmonary events.

12.2.3.15 Malignancies of Donor Origin

The development of malignancies of donor origin was specifically noted as a risk in the safety assessment of umbilical CB (FDA 2013).

No cases of new malignancies were reported during the one year follow-up of this study. Long-term follow-up of the study patients up to 5 years post-transplant was ongoing at the time of this report. Two patients treated with omidubicel and one patient treated with unmanipulated CBU on study P0501 developed new malignancies in the long-term follow-up (LTFU) – the two omidubicel recipients developed post-transplant lymphoproliferative disorder (PTLD), the unmanipulated CBU recipient was diagnosed with a new malignancy.

GP3LOY-003 was an African American female, aged 47 at transplant, with a primary diagnosis of high-risk T-lymphoblastic leukemia (failure to achieve CR after first induction). The patient was transplanted with omidubicel and achieved neutrophil engraftment on Day 14, however the patient relapsed 252 days following transplantation, and was re-treated with chemotherapy. The patient's disease responded and maintained donor chimerism, however remained cytopenic. Following rising EBV PCR copies, the patient was diagnosed with Monomorphic PTLD, Diffuse Large B-Cell Lymphoma (activated B-Cell type), 523 days following transplantation. PTLD was treated with Rituximab initially, and subsequently with lenalinomide, cyclophosphamide with dexamethasone, ibrutinib, and brentuximab. However, the disease progressed, and the patient died 603 days following transplantation. The primary cause of death was listed as PTLD with secondary causes listed as multi-system organ failure and bacterial infection.

GP3UMN-001 was aged 24 at transplant, a Caucasian male with a primary diagnosis of early T-cell precursor ALL (ETP-ALL). The patient was transplanted with omidubicel and achieved neutrophil engraftment on Day 8. The post-transplant course was complicated by Grade III acute GvHD, followed by moderate chronic GvHD, which worsened to severe on LTFU. The patient initially developed EBV viremia on the P0501 and was treated with Rituximab. Viremia was resolved by one-year post-transplant. However, during the LTFU a mass in the frontal cerebral lobe was diagnosed to be Monomorphic PTLD EBV positive DLBCL, 615 days following transplantation. The patient was treated with Rituximab and radiation therapy. Subsequent follow-up indicated remission with negative EBV with no sign of progression up to the last follow-up, approximately four months before the cutoff.

PTLD is a known severe complication of transplantation, that occurs in up to 11% of HSCTs with mismatched unrelated donor sources (Compagno, Basso et al. 2020). Cord blood transplantation is specifically associated with a greater risk of PTLD, due to low numbers and naiveté of infused T-cells. PTLD in the HSCT setting are almost exclusively related to EBV infection. All these risk factors were shared by patients GP3LOY-003 and GP3UMN-001. Additional risk factors include the chemotherapy given to GP3LOY-003 for relapsed T-

cell ALL and subsequent cytopenia, and prolonged immunosuppression given to GP3UMN-001 for protracted GvHD (Al-Mansour, Nelson et al. 2013).

One patient treated with unmanipulated CBU developed a malignancy that was assessed to be of donor cell origin. Patient GP3UTR-002 was a 17 year-old female, with a history of ALL. Approximately 35 months following transplantation, the patient was diagnosed with new leukemia. Bone marrow could not be assessed due to a concurrent fungal infection that led to patient's death on the day of leukemia diagnosis. Testing on residual lab material indicated 100% donor chimerism.

Donor cell derived leukemias are a known and serious complication of allogeneic HSCT (Wiseman 2011). The reported incidence varies between 0.12 – 5% among allogeneic HSCT recipients and has specifically been reported for CBT (Hertenstein, Hambach et al. 2005, Greaves 2006, Ruiz-Argüelles, Ruiz-Delgado et al. 2006, Flynn and Kaufman 2007, Nagamura-Inoue, Kodo et al. 2007, Wang, Hutchinson et al. 2011). Donor cell derived myelodysplastic syndrome has also been described, and the rate of transformation to leukemia is unknown. The etiology of donor cell leukemia is unclear, and multifactorial processes have been described, involving either donor cell related abnormalities, or recipient factors that are also exacerbated by impaired immune surveillance and other toxic effects of post-transplant care (Cooley, Sears et al. 2000, Wiseman 2011). Cord blood or prenatal derived abnormal clones have also been implicated as potential preleukemic triggers (Maeda, Ohno et al. 1991, Gale, Ford et al. 1997, Uckun, Herman-Hatten et al. 1998, Wiemels, Cazzaniga et al. 1999, Wiemels, Xiao et al. 2002, Greaves 2006). The natural history for malignancy of donor origin is presumed to be the same as that for *de novo* leukemia.One patient treated with omidubicel had a Grade 3 increase in T-lymphocyte counts (clonal T-cell lymphocytosis) reported as a possibly related SAE (patient GP3CCF-002). This patient was a 40-year-old White female with CML. The patient engrafted neutrophils six days post-transplant, and platelets 25 days post-transplant. Approximately two months following transplant, lymphocytosis was noted during the assessment of CMV viremia, which was found to be monoclonal. The CMV infection cleared with treatment, however the lymphocytosis persisted over time without clinical sequelae. A detailed narrative for this patient is provided in Section 12.2.6.

There was no evidence of malignancy throughout two years of surveillance, and no further intervention was required for this patient.

12.2.3.16 Potential Class Effect: Cytokine Release Syndrome and Neurological Toxicities

There were no reports of cytokine release syndrome in the omidubicel treatment group. Of the 52 patients treated with omidubicel, nervous system disorders included the following events presented in Table 42.The data did not indicate any particular risk for neurological toxicities, above the overall known profile of toxicities following myeloablative conditioning, HSCT and supportive treatments.

Table 42: Nervous System Disorders in Patients Treated with Omidubicel

Preferred Term	Patients (N)	Grade
Dysgeusia	15	Grade 1/2
Dizziness/somnolence	14	Grade 3; n=1 Grade 1/2 n=13
Tremor	8	Grade 1/2
Syncope	3	Grade 3
Peripheral neuropathy	3	Grade 1/2
Subarachnoid hemorrhage	2	Grade 3 n=1 Grade 1 n=1
Facial paresis	1	Grade 1
Dysarthria	1	Grade 2

Data Source: Listing 16.2.7.8

N= Total number of patients with nervous system disorders by Preferred Term; n= Number of patients with nervous system disorders for each Preferred Term by grade

12.2.4 Listing of AEs by Patient

All AEs are detailed by patient in Listing 16.2.7.8.

12.2.5 Deaths, Other Serious Adverse Events, and Other Significant AEs

12.2.5.1 Deaths

A total of 42 deaths were reported (Listing 16.2.7.1) during the main study follow-up. Seventeen deaths occurred in patients randomized to omidubicel, and 25 deaths occurred in patients randomized to unmanipulated CBU. Of these, two patients on the omidubicel arm and three patients on the unmanipulated CBU arm died of disease relapse before transplant.

In the SP, deaths were reported for 12 (23%) patients treated with omidubicel and 20 (36%) patients treated with unmanipulated CBU. Among patients treated with omidubicel, common causes of death were infections, acute GvHD, and relapse (n=3 for each). One patient each died of pulmonary hemorrhage, thrombotic microangiopathy, and veno-occlusive disease/sinusoidal obstruction syndrome. In patients treated with unmanipulated CBU, the most common causes of death were infection or septic shock (n=6), respiratory disorders (n=6; including hypoxic respiratory failure, ARDS, idiopathic pneumonia, and pulmonary organ failure), disease relapse (n=4), and GvHD (n=3). One patient died of veno-occlusive disease/sinusoidal obstruction syndrome.

The following interpretations were made in determining the above descriptions of causes of death:

- The primary cause of death for two patients (GP3SGH-001, GP3SGH-002) was recorded as acute leukemia/prior malignancy due to site's convention, however the actual cause of death was a respiratory failure for both. The primary cause of death for one patient (GP3LAF-001) was suicide, but the cause of death was summarized according to the secondary cause of death which was relapse.

- The primary cause of death for one patient (GP3SGH-007) was reported as acute subdural hemorrhage, however this event was a manifestation of disease relapse and the fatal SAE was recorded as disease relapse. Therefore, the cause of death was summarized according to this.

Deaths after main study follow-up as of data cutoff (April 29, 2021)

Patients who consented to the LTFU sub-study of this protocol are followed for up to 5 years post-transplant to report new deaths and other major outcomes occurring during standard of care follow-up. As of the data lock for this report, eight patients had died during LTFU:

- Omidubicel arm
    - GP3CCF-006 (04May2019) – Died at 16 months due to viral encephalitis.
    - GP3DFC-001 (26Jan2018) – Died at 23 months due to viral infection.
    - GP3HSP-001(17Dec2018) – Died at 27 months due to multi-system organ failure. Relapse reported at month 23.
    - GP3LOY-003 (28Sep2018) – Died at 20 months due to PTLD. Secondary causes included multi-system organ failure and bacterial infection.
    - GP3LOY-007 (06Mar2019) – Died at 21 months due to relapse. Secondary causes include viral and bacterial infections. Relapse occurred on the primary study at month 3.
    - GP3UMN-005 (07Nov2018) – Died at 19 months due to relapse. Relapse occurred on the primary study at month 9.
- Unmanipulated CBU arm
    - GP3PMC-001 (10Apr2021) – Died at 28 months due to relapse.
    - GP3UTR-002 (26Mar2021) – Died at 34 months from fungal infection (pulmonary aspergillosis). Relapse diagnosed on day of death.

12.2.5.2 Other Serious Adverse Events

All SAEs are presented in Listing 16.2.7.7.

12.2.5.3 Other Significant AEs

No other significant AEs were observed during this study.

12.2.6 Narratives of Deaths, Other Serious Adverse Events, and Certain Other Significant AEs

Narratives for patients who had SAEs are provided in Section 14.3.1. While this CSR summarizes the study data up to April 29, 2021 (at which point all patients reached 365 Days

post-transplant / 15 Months post-randomization), the narratives include additional summaries of safety events reported until the cutoff of October 20, 2021.

12.3 Clinical Laboratory Evaluation

12.3.1 Listing of Individual Laboratory Measurements by Patient and Each Abnormal Laboratory Value

Listings of individual laboratory measures for serum chemistry are provided in Listing 16.2.8.1.

12.3.2 Evaluation of Each Laboratory Parameter

Summaries of hematology and chemistry values at each protocol-defined timepoint are provided in Table 14.3.7.2.

Clinical laboratory abnormalities are summarized in Table 14.3.7.3. All patients on the study experienced at least one laboratory abnormality. Of these, hypomagnesemia occurred in 96% of patients in both groups, hypoalbuminemia occurred in 90% of omidubicel patients and 98% of unmanipulated CBU, hypocalcemia occurred in 83% of omidubicel patients and 95% of unmanipulated CBU patients, and hyperglycemia occurred in 85% of omidubicel patients and 77% of unmanipulated CBU patients.

All treatment emergent clinically significant Grade 3-5 abnormalities and SAEs were considered as TEAEs and are described throughout 12.2.3.

The most commonly reported clinically significant Grade 3-5 laboratory adverse events in patients treated with omidubicel on Study P0501 included hypokalemia in 6 (12%) patients, hyperglycemia and transaminases increased in 4 (8%) patients each. Among patients treated with unmanipulated CBU, common events included hyperglycemia in 8 (14%) patients, hypokalemia and hypophosphatemia in 5 (9%) patients.

Overall, while lab abnormalities occurred in almost all treated patients, laboratory related adverse events deemed clinically significant were infrequently reported. Moreover, laboratory AEs occurred at a similar rate in both omidubicel and unmanipulated CBU groups, or in lower numbers in omidubicel patients, and did not indicate a potential safety issue, beyond the known toxicity prevalent in patients with underlying severe hematologic malignancies with prior treatments, undergoing myeloablative conditioning followed by HSCT.

12.4 Vital Signs, Physical Findings, and Other Observations Related to Safety

12.4.1 Vital Signs

A summary of vital signs at each protocol-defined timepoint are presented in Table 14.3.7.4.

A by-patient listing of vital sign results is provided in Listing 16.2.8.3.

Hypertension was reported as an adverse event for 90% of omidubicel patients and 88% of unmanipulated CBU patients (Table 14.3.7.5). The occurrence of Grade 3 treatment-emergent hypertension is summarized and discussed in Section 12.2.3.13. Pyrexia was reported for 85% of omidubicel patients and 96% of unmanipulated CBU patients. In the post HSCT setting, pyrexia is most often associated with infections, which are assessed in Section 12.2.3.10.

There were no clinically significant differences between treatment groups in vital sign parameters.

12.5 Safety Conclusions

In summary, the main conclusions of the safety analyses indicate a similar frequency and severity of Grade 3 and above infusion reactions observed in patients treated with omidubicel compared to unmanipulated CBU. Overall the frequency of Grade 3 or higher TEAEs was either similar or lower for omidubicel than for unmanipulated CBU. A review of these events noted a higher frequency of pain reported for the omidubicel recipients, however further interrogation of the safety data did not indicate an underlying safety event that occurred at a higher frequency or severity for omidubicel recipients. Patients randomized to omidubicel had a lower incidence of Grade 2-3 bacterial or invasive fungal infections by 100 days following transplantation compared to patients randomized to unmanipulated CBU (39% vs. 60%). The risk ratio for total infections, bacterial infections or viral infections was significantly lower for omidubicel compared to unmanipulated CBU, irrespective of disease severity. Patients transplanted with omidubicel had fewer infectious SAEs and a lower incidence of fever and sepsis. A higher frequency and severity of respiratory events was reported in the unmanipulated CBU group, especially respiratory failure. In further analysis, the majority of these events occurred concurrently or were attributable to infectious complications.

The outcomes of acute and chronic GvHD demonstrated no statistically significant difference between patients transplanted on the omidubicel or the unmanipulated CBU groups. These rates are consistent with those observed with other graft modalities used in HSCT. There was no significant difference in the risk of relapse among the two arms. No cases of new malignancies of donor origin were reported in the study.

Allogeneic HSCT following myeloablative conditioning is associated with a well-described pattern of severe, life-threatening or fatal complications. Many of the toxicities associated with HSCT are related to the duration of hematopoietic recovery after transplant. The rapid rate of hematopoietic recovery observed in patients transplanted with omidubicel was associated with clinically meaningful improvement in infection rates and duration of hospitalization. The overall pattern and severity of AEs, as well as treatment-related mortality, were more favorable in patients treated with omidubicel than in those treated with standard cord.

Patients transplanted with omidubicel are potentially at risk of developing toxicities which may occur following HSCT with other graft sources. Safety data demonstrated that safety

outcomes were consistent with those observed with myeloablative HSCT with other graft sources.

13 DISCUSSION AND CONCLUSIONS

13.1 Discussion

The purpose of this Phase III pivotal study was to compare the efficacy and safety of omidubicel with the most relevant comparator, standard unmanipulated umbilical CB, from which it is derived. This study was designed to evaluate these objectives in patients with high-risk hematologic malignancies who required allogeneic HSCT and did not have a suitable matched donor available in a timely manner.

Omidubicel is a cryopreserved allogeneic umbilical cord blood-derived, stem cell-based product comprised of *ex vivo* expanded hematopoietic CD34+ progenitor cells and non-expanded mature myeloid and lymphoid cells. Omidubicel was formulated as a cellular suspension for IV infusion a minimum of 5.6×10^7 CD34+ cells and a minimum of 2.4×10^7 CD3+ cells.

Both study arms utilized the same type, quantity and quality of donor stem cells derived from CBUs selected prior to randomization. As this study was conducted in an orphan patient population, it was imperative to investigate the safety and tolerability of omidubicel in a diverse population representative of patients with high-risk hematologic malignancies. Patients were randomized by minimization to balance the groups for the most important prognostic factors impacting treatment outcomes. Considering the diversity of the patient population in terms of age, primary diseases, disease risk and specific clinical site supportive care guidelines, randomization was conducted successfully, as demonstrated by well-balanced patient characteristics across the two study arms. As noted, the diversity of the patient population was substantial, with ages spanning 13-65 years, weights of 43-134 kg, six major diagnoses with varying disease risk and numerous specific diseases. This wide range reflects a population that is representative of the general population eligible for transplant. Importantly, the study population was ethnically diverse, with over 40% identified as non-Caucasian. While many Caucasian patients are able to find suitable donors within the registries, these ethnically diverse populations have a much lower success rate and represent the highest need for better graft alternatives.

Most importantly, the primary endpoint was a clinically meaningful and objective endpoint, as reflected by serial daily blood counts and the median time to engraftment of 12 days, representing an effect of clinical significance. The primary analysis of the primary endpoint was an ITT analysis, encompassing all randomized patients according to their originally assigned treatment. As such, although the analysis assessed a post-transplant measure, it included all the treatment failures, treatment deviations and patients who were not treated. This approach minimized the risk of bias due to knowledge of the treatment assignment, given that patients and clinical study sites were not blinded to treatment allocation. Furthermore, this approach preserved the prognostic balance across the two arms. While the three-week duration required for omidubicel production could have been associated with an increased risk of relapse prior to transplant in this arm, the ITT analysis reflected a comprehensive assessment of the treatment benefit and revealed no such risk.

The secondary endpoints in this study were incidence of Grade 2/3 bacterial or invasive fungal infections by 100 days following transplantation, days alive and out of hospital in the

first 100 days following transplantation, and platelet engraftment by 42 days following randomization. Similar to the primary endpoint, although these events all assess post-transplant complications, they were primarily analyzed on the ITT population, with the analysis methods encompassing also events that occurred between randomization and transplantation, for a more comprehensive assessment of the treatment.

Bacterial and fungal infections predominate in the early months after transplant and are dependent on rapid and robust neutrophil recovery (Hamza, Lisgaris et al. 2004, Yazaki, Atsuta et al. 2009). Consistently with this, recipients of umbilical CB transplants required longer durations of hospital stay compared to patients transplanted with other graft sources in a study of length of stay in the first 100 days after HSCT in 1577 patients with acute leukemia undergoing HSCT. For adults receiving HSCT using myeloablative conditioning, median days alive and OOH in the first 100 days were 52 days for single umbilical CB, 55 days for double umbilical CB, 69 days for MUD BM, 75 days for peripheral blood stem cells (PBSC) MUD, 63 days for MMUD BM and 67 days for MMUD PBSC recipients (Ballen, Joffe et al. 2014). Overall, the secondary endpoints of this study reflected the significant risk of clinical sequelae of delayed hematopoietic recovery. Results of the secondary endpoint analyses supported the primary endpoint analysis and provided further evidence of the clinical benefit of omidubicel. Other study endpoints, as well as additional analyses performed, further assessed engraftment, infections and hospitalization and provided a comprehensive and robust picture of benefit in these topics.

The safety findings were overall consistent with the known toxicities and complications following allogeneic HSCT with associated conditioning therapy, with some indications of an improved safety profile for omidubicel over unmanipulated CBU transplants. The frequency and severity of the main post-transplant complications were either reduced for omidubicel recipients, as in the case of infections, or were similar to the known experience, as in the case of GvHD.

Overall, the results from this well-conducted pivotal Phase III study, as demonstrated by well-balanced patient characteristics, and an ITT analysis of the primary and secondary endpoints, support the rationale for the clinical use of omidubicel in this patient population. Moreover, results from this study were consistent with findings from early phase clinical studies and establish the overall risk-benefit profile, which appears to be favorable.

13.2 Conclusions

This study was designed to compare the efficacy and safety of omidubicel with the most relevant comparator, standard umbilical CB, from which it is derived. Both study arms utilized the same type, quantity and quality of donor stem cells derived from CBUs selected prior to randomization.

Overall results demonstrate omidubicel has the potential to provide a life-saving graft for a diverse group of patients in need of HSCT. This randomized, well controlled study met its primary endpoint, demonstrating a significant improvement in time to neutrophil engraftment. The primary endpoint was supported by secondary endpoints that demonstrated significant improvement (with multiplicity adjustment) in Grade 2/3 bacterial and invasive fungal infections, days alive and out of hospital, and platelet engraftment following transplantation. The secondary endpoints reflected the significant risk of clinical sequelae of

delayed hematopoietic recovery, and results from the secondary endpoint analyses support the primary endpoint analysis, providing further evidence of the overall clinical benefit of omidubicel.

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14.3.1 Narratives of Deaths, Other Serious and Certain Other Significant AEs

Subject Identifier	GP3BCH-001
Age	14
Sex	Male
Baseline Weight (Kg)	49.6
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	07 Dec 2018
Event	Disease Progression
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	13 Sep 2018 – 05 Nov 2018
Outcome Of Event	Resolved
Relationship To The Study Drug	NA: Pre-transplant event
Date Of Death (If Applicable)	

Narrative:

Patient GP3BCH-001 is a 14 year-old White male with ALL who received a Omidubicel transplant on 07-Dec-2018.

The patient was diagnosed with ALL (Pre-B-ALL with MLL translocation t(11, 19) (q23, p13) by FISH and cytogenetics 47 XY +X t(11, 19) (q23, p13) [17]/46 XY [3]) on 10-Nov-2016. The patient received induction and consolidation therapy per Dana-Farber Cancer Institute (DFCI) treatment protocol 11-001 (induction: 10-Nov-2016 to 20-Dec-2016; consolidation 1a: 21-Dec-2016; consolidation 1b: 13-Jan-2017; consolidation 1c: 02-Feb-2017, CNS phase 23-Feb-2017; consolidation II: 30-Mar-2017). Maintenance therapy was given from 16-Nov-2017 to 06-Jul-2018. The patient had early combined marrow/CNS relapse on 06-Jul-2018 for which he was treated with intrathecal (IT) methotrexate, cytarabine, and hydrocortisone from 06-Jul-2018 to 27-Jul-2018. He was treated with Capizzi reinduction starting on 07-Aug-2018. The patient was in CR2 at study screening. The patient's past medical history included *Candida* mucositis. He had a history of mild hepatic impairment from 22-Oct-2018 to 04-Nov-2018 (UNL 1.2) and moderate/severe hepatic impairment from 17-Sep-2018 to 19-Sep-2018 (1.5 > UNL) that was absent at study screening.

Based on the screening BM examination performed prior to study consent (12-Jul-2018), the patient was eligible for the study trial and ready for randomization. Although randomized to the study trial, the patient did not initially receive the study product as he was diagnosed with disease progression on 13-Sep-2018 during the randomization segment of the study trial. Post-randomization BM flow cytology revealed remission morphology but 15% abnormal B-lymphoblasts requiring further treatment.

The patient was put on holding cycle with cyclophosphamide, cytarabine, IT-methotrexate, and 6-MP. Cycle 1 blinatumomab was started on 04-Oct-2018 for 28 days, IT-methotrexate on Day 15, and dexamethasone days 1-8. Cycle 2 blinatumomab was started on 09-Nov-2018 for 2 weeks. A BM aspiration done on 05-Nov-2018 showed no abnormal lymphoblasts. The disease progression event was reported as resolved as of 05-Nov-2018.

Prior to omidubicel transplant, the patient was then treated with a myeloablative conditioning regimen consisting of TBI (03-Dec-2018 to 06-Dec-2018), fludarabine (30-Nov-2018 to 02-Dec-2018), and cyclophosphamide (30-Nov-2018 to 01-Dec-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. The patient received the omidubicel transplant on 07-Dec-2018. Neutrophil counts recovered at 17 days post-transplantation (24-Dec-2018). The patient was discharged from the hospital on 04-Jan-2019. The site reported no SAEs post-transplantation.

The site did not report all relapse events as SAEs, but since the protocol-defined relapse as a medically important event, the information has been provided.

The patient presented to clinic on 07-Oct-2019 with bruising noted by a caregiver over the past few weeks. Bruising initially presented on his legs but was also noted on his arms. CBC was drawn which revealed a WBC

count of 55 x 10^9/L with more than 75% blasts, hemoglobin of 10.9 g/dL, and a platelet count of 8 x 10^9/L. Uric acid was elevated at 8.3 mg/dL as was the lactate dehydrogenase (LDH) (696 U/L). Due to the concern for relapsing disease and tumor lysis syndrome, the patient was admitted to the hospital for further management. A chest X-ray performed prior to admission was negative for a mediastinal mass or consolidation. The patient had also noted some intermittent numbness bilaterally on the lower lip as well as a dry cough.

The patient started treatment on 10-Oct-2019 with chemotherapy according to Children's Oncology Group (COG) protocol AALL1231 (weekly vincristine and daunorubicin with dexrazoxane starting on Day 1, dexamethasone on days 1-28, and asparaginase on Day 4). A BM exam performed on 11-Oct-2019 confirmed relapse of disease with 92% blasts.

The disease was found to be refractory to treatment on 07-Nov-2019 so another round of induction was administered according to protocol 17-617 on 15-Nov-2019 consisting of venetoclax, cytarabine, etoposide, and asparaginase. As of the last study-related follow-up on 11-Dec-2019, a second cycle of reinduction was planned to begin on 13-Dec-2019. This disease relapse event was considered to be resolved by convention as it was ongoing at the end of study follow-up.

Subject Identifier	GP3BCH-002
Age	20
Sex	Male
Baseline Weight (kg)	95.0
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	19 Jul 2019
Event	1. Viral Encephalitis 2. Diarrhea 3. AKI 4. Hypertension
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 04 Oct 2019 – 18 Oct 2019 2. 28 Oct 2019 – 24 Nov 2019 3. 06 Nov 2019 – 29 Nov 2019 4. 06 Nov 2019 – 29 Nov 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No
Date Of Death (If Applicable)	
Narrative: Patient GP3BCH-002 is a 20 year-old White male with ALL who received an Unmanipulated CBU transplant on 19-Jul-2019.	

The patient was diagnosed with ALL on 18-Oct-2017. He underwent induction therapy with COG protocol AALL1131 starting 19-Oct-2017, was switched to AALL1631 for induction days 15-29, and received induction starting 18-Nov-2017 through day 28. The patient received high-dose methotrexate interim maintenance therapy (AALL1631 investigational arm B) starting 22-Jan-2018 through day 45, had delayed intensification (26-Mar-2018) through day 21, and delayed intensification part 2 (11-May-2018) through day 50. He was continued on Capizzi methotrexate interim maintenance therapy (12-Jun-2018) through day 41, maintenance cycle 1 (09-Aug-2018) through day 78, maintenance cycle 2 (01-Nov-2018) through day 78, and maintenance cycle 3 (24-Jan-2019) through day 8. He was found to have isolated CNS relapse (90% blasts in CSF collected) on 24-Jan-2019. The patient had an individualized reinduction/salvage therapy treatment plan (references: COG protocols AALL1131 and AALL02P2) starting on 01-Feb-2019 through 22-Feb-2019. This included dexamethasone 5 mg/m2/dose BID (days 1-14), vincristine 1.5 mg/m2/dose (days 1, 8, 15, 22), daunorubicin 25 mg/m^2 (days 1, 8, 15), dasatinib 60 mg/m^2 (days 1-29), and triple intrathecals twice weekly (methotrexate 15 mg, hydrocortisone 15 mg, and cytarabine 30 mg; days 1, 4, 8, 11, 15, 22). The patient's past medical history included insulin dependent diabetes due to necrotizing pancreatitis and obesity. He had moderate/severe hepatic impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (15-Jul-2019 to 18-Jul-2019), fludarabine (11-Jul-2019 to 13-Jul-2019), and cyclophosphamide (11-Jul-2019 to 12-Jul-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included pentamidine, acyclovir, ciprofloxacin, and fluconazole. Neutrophil counts recovered at 21 days post-transplantation (09-Aug-2019). The patient was discharged from the hospital on 21-Sep-2019.

The patient was admitted on 04-Oct-2019 for fever, altered mental status, hyponatremia, and hyperglycemia. The CSF was found to be concerning for highly reactive viral encephalitis/meningitis. CSF culture was negative for HHV6 but a blood sample showed 2900 copies/mL. The patient completed treatment with ganciclovir (treatment dosing) which started on 08-Oct-2019. He was discharged on 18-Oct-2019 and continued prophylactic valgancyclovir.

The patient was then admitted on 28-Oct-2019 for increased diarrhea, abdominal cramping, left-sided abdominal pain, fatigue, and lightheadedness. A CT scan of the abdomen and pelvis on 30-Oct-2019 showed no evidence of intestinal inflammation, infection, or GvHD. Stool was found to be positive for *C. difficile* for which he was treated with vancomycin. On 06-Nov-2019 hospitalization was prolonged due to increasing creatinine (2.22 mg/dL), refractory hypertension (maximum 167/120), elevated LDH (in the range of 600 U/L), and decreasing hemoglobin (8 g/dL). The patient was discharged home on 29-Nov-2019 with clonidine patch and nifedipine. Due to symptom resolution, GI scoping was not necessary.

Subject Identifier	GP3CAL-001
Age	62
Sex	Female
Baseline Weight (kg)	49.7
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	22 Apr 2019
Event	No SAEs Reported
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	
Narrative: Patient GP3CAL-001 is a 62 year-old White, North American female with Myelodysplastic Syndrome who received a Omidubicel transplant on 22-Apr-2019.	

The patient was diagnosed with Myelodysplastic Syndrome (MDS) on 30-Jul-2018. She underwent induction therapy with decitabine for three cycles from 03-Sep-2018 to 30-Nov-2018, and three additional cycles from 14-Jan-2019 to 30-Mar-2019. The patient's past medical history included chronic back pain, thoracic/lumbar spondylosis, left-sided sciatica, anxiety, depression, hyperlipidemia, internal hemorrhoids, gastroesophageal reflux disease, arthritis, prediabetes, urinary incontinence, exercise induced ischemia, fatigue, leukopenia, thrombocytopenia, anemia, vitiligo, vulvar lichen sclerosis, recurrent *E.coli* urinary tract infections, headaches, chronic right lower quadrant abdominal pain, and neutropenic sepsis. She had moderate pulmonary impairment at study screening. Surgical history included hemorrhoid band ligation, exploratory laparoscopy, nephrolithiasis surgical removal, left knee surgery, hernia repair, bladder dilation, and bilateral breast implantation.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (17-Apr-2019 to 19-Apr-2019), thiotepa (15-Apr-2019 to 16-Apr-2019), and busulfan (17-Apr-2019 to 19-Apr-2019). GvHD prophylaxis included mycophenolate mofetil, cyclosporine, and immune globulin. Infection prophylaxis included acyclovir, posaconazole, levofloxacin, ganciclovir, nystatin, and cotrimoxazole. Neutrophil counts recovered at eight days post-transplantation (30-Apr-2019). The patient was discharged from the hospital on 19-May-2019. There were no SAEs reported post-transplantation.

Subject Identifier	GP3CAL-002
Age	59
Sex	Male
Baseline Weight (kg)	71.7
Race	Asian - Chinese
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	27 Aug 2019
Event	BK Virus Cystitis
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	06 Nov 2019 – 07 Nov 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3CAL-002 is a 59-year-old Asian, Chinese male with ALL who received an Unmanipulated CBU transplant on 27-Aug-2019.

The patient was diagnosed with acute lymphoblastic leukemia (BCR-ABL positive ALL) on 02-Jan-2019. He underwent induction therapy with hemophagocytic lymphohistiocytosis (HLH) protocol starting on 04-Jan-2019 (etoposide, dexamethasone, dasatinib, and a short course of cyclosporin A). Bone marrow biopsy on 21-Jan-2019 showed hypocellular marrow, occasional hemophagocytic histiocytes, and 3-4% of blasts positive for BCR-ABL. The patient was then treated with single agent dasatinib starting 25-Jan-2019. Bone marrow biopsy on 14-Mar-2019 was normocellular, with no excess blasts, and normal cytogenetics. The patient was then started on Berlin-Frankfurt-Munich (BFM) induction (minus PEG) on 08-Apr-2019. On 06-May-2019, BM biopsy found normocellular marrow, hemophagocytosis, and low level ABL1-BCR (9;22) fusions. The patient then underwent consolidation therapy with BFM starting on 21-May-2019. The patient's past medical history included asthma, left genicular and peroneal acute thrombi, gastroesophageal reflux disease, hemophagocytosis of liver sinusoids, anemia, hemophagocytic lymphohistiocytosis, peripheral neuropathy, dysgeusia, intermittent constipation, intermittent nausea, weight loss, hypertension, insomnia, dry eyes, and lactose intolerance. He had mild hepatic and moderate pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (22-Aug-2019 to 24-Aug-2019), thiotepa (20-Aug-2019 to 21-Aug-2019), and busulfan (22-Aug-2019 to 25-Aug-2019). GvHD prophylaxis included mycophenolate mofetil and

cyclosporine. Infection prophylaxis included acyclovir, cotrimoxazole, ganciclovir, levofloxacin, nystatin, and posaconazole. Neutrophil counts recovered at 29 days post-transplantation (25-Sep-2019). The patient was discharged from the hospital on 25-Sep-2019.

The patient presented to the ED on 06-Nov-2019 with worsening dysuria and urinary frequency for one week. He reported nausea and vomiting (no blood) but denied back pain, flank pain, abdominal pain, fever, or chills. Vital signs in the ED were T 36.8°C, HR 103, BP 142/104, RR 18, and O_2 saturation of 97% on room air. The patient was given ceftriaxone. On 07-Nov-2019 the patient was diagnosed BK virus cystitis (>140,000,00 copies on 05-Nov-2019). The patient continued to experience dysuria without gross hematuria. He was discharged home on 07-Nov-2019 with baclofen and phenazopyridine for symptomatic management. He was referred to outpatient urology management for irrigation depending on BK cystitis course trajectory.

Subject Identifier	GP3CAL-003
Age	33
Sex	Female
Baseline Weight (kg)	54.0
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	04 Oct 2019
Event	1. Severe Hypotonic Hyponatremia 2. Multiple Organ Failure 3. Hypoxemic Respiratory Failure 4. VOD 5. PGF
Severity	1. Grade 3 2. Grade 4 3. Grade 4 4. Grade 5 5. Grade 4
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 28 Sep 2019 – 30 Sep 2019 2. 21 Oct 2019 – 17 Nov 2019 3. 06 Nov 2019 – 17 Nov 2019 4. 22 Oct 2019 – 17 Nov 2019 5. 16 Nov 2019 – 17 Nov 2019
Outcome Of Event	1. Resolved 2. Death 3. Death 4. Death 5. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. No 3. No 4. No 5. Yes
Date Of Death (If Applicable)	17 Nov 2019
Narrative: Patient GP3CAL-003 is a 33 year-old White female with Acute Myelomonocytic Leukemia who received an Unmanipulated CBU transplant on 04-Oct-2019.	

The patient was diagnosed with favorable risk AML, M4, NPM1+, and normal cytogenetics) on 02-Oct-2014. She underwent induction therapy with 7+3 cytarabine and idarubicin (09-Oct-2014 to 02-Dec-2014). Consolidation therapy included four cycles of HiDAC initiated on 02-Dec-2014. The patient achieved complete remission but was lost to follow-up for two years. A BM biopsy on 10-Jun-2019 showed a hypocellular marrow with multilineage dysplasia and excess myeloblasts (5-8%) confirming late disease relapse. The disease was considered high-risk and was characterized by complex karyotype, TP53, deletion 5q, and monosomy 7. The patient received reinduction chemotherapy starting on 14-Jun-2019 with 7+3 (cytarabine and daunorubicin). Response was appropriate, with a hypocellular marrow with no excess blast on day 14 of induction. A BM exam performed on 12-Jul-2019 revealed a variably cellular marrow without excess blasts and with the previously detected TP53. Consolidation therapy with HiDAC was administered from 02-Aug-2019 through 07-Aug-2019. A second complete remission was confirmed on 10-Sep-2019. The patient's past medical history included HSV-2 seropositivity, thrombocytopenia, primary ovarian insufficiency, deviated septum, anemia, recurring sinusitis, anxiety, anaclitic depression, pain syndrome, elevated alkaline phosphatase, elevated blood glucose, insomnia, headaches, and hypomagnesemia.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 40 mg/day (26-Sep-2019 to 28-Sep-2019), cyclophosphamide 3336 mg/day (27-Sep-2019 to 28-Sep-2019), and TBI 150 cGy/day (30-Sep-2019 to 03-Oct-2019). GvHD prophylaxis included mycophenolate mofetil, cyclosporine, and immune globulin (IVIG). Infection prophylaxis included ganciclovir, acyclovir, letermovir, posaconazole, nystatin, isavuconazole, levofloxacin, and cotrimoxazole.

During the conditioning regimen, the patient was transferred to the MICU on 28-Sep-2019 for asymptomatic hyponatremia (121 mEq/L). The condition was likely syndrome of inappropriate antidiuretic hormone secretion (SIADH) given the serum osmolality (251 mmol/kg), urine sodium (51 mEq/L), and urine osmolality (440 mmol/kg). Given the presentation, cyclophosphamide was considered the likely cause as the sodium level prior to the first infusion was 140 mEq/L but rapidly decreased to 121 mEq/L by the next evening. Cyclophosphamide infusions were completed, and the patient was treated with sodium chloride tablets and fluid restriction. Sodium levels corrected (131 mEq/L then 138 mEq/L) following treatment so the patient was transferred back to the transplant unit. She received the double cord blood transplant as planned on 04-Oct-2019.

The patient was transferred to the MICU on 21-Oct-2019 due to encephalopathy and signs of multi-organ failure: acute liver failure (met all triad: abnormal liver tests, encephalopathy, international normalized ratio (INR)>1.5), anuric AKI, coagulopathy (liver disseminated intravascular coagulation), lactic acidosis, neutropenic fever likely due to mucositis, and hyperbilirubinemia. The presentation was concerning for sinusoidal obstruction syndrome (SOS). The renal failure required initiation of inpatient hemodialysis (HD). Liver failure was thought to be secondary to VOD; therefore, the patient was started on defibrotide and ursodiol. The patient's liver function slowly recovered but bilirubin levels continued to be elevated. The patient was started on Vitamin K for elevated INR. Renal function improved slightly (urine output of 300-400 cc/day) so the patient was transitioned to intermittent HD. There was also an apparent improvement in mental status. The patient was continued on isavuconazole and meropenem for concerns of sepsis. Her PICC line was removed on 31-Oct-2019 and a Hickman central venous line (CVL) was placed on 01-Nov-2019. A BM biopsy was performed at the same time. The patient was then transferred back to the transplant unit in stable condition.

The patient attempted suicide on 05-Nov-2019. Following the attempt and after taking oral medication with water, the patient had a coughing episode for which she required supplemental oxygen. The patient was started on nebulizer treatments but was noted to have increasingly labored breathing and difficulty clearing secretions. She was transferred to the MICU with hypoxemic respiratory failure on 07-Nov-2019. Upon transfer, the patient was intubated given persistent desaturation and increased work of breathing. Initially the patient continued to desaturate to 85-88% on volume control (VC) 420, respiratory rate (RR) 20, FIO2 100%, and PEEP 5. She had worsening oxygen saturation with PEEP 10 and appeared to be dyssynchronous with the ventilator. Ventilation status improved with fentanyl administration. The patient was started on a norepinephrine drip and CRRT with volume removal. A post-intubation chest x-ray showed whiteout of the left lung likely consistent with a mucus plug. Respiratory status improved with suctioning, albuterol, ipratropium, and mucomyst. Final ventilator settings were PC 12, RR 20, FIO2 60%, and PEEP 10.

Chimerisms by peripheral blood were obtained per protocol on 01-Nov-2019 (post-transplant day +28) and 15-Nov-2019 (post-transplant day +42) which revealed CBU #2 at 97% and host cells at 3% for both assessments. Neutrophils did not engraft by day 42, confirming PGF on 15-Nov-2019.

The patient died on 17-Nov-2019. Primary cause of death was noted as organ failure, resulting from VOD/SOS.

Deviations with potential medical significance: The patient's mycophenolate mofetil dose was 750 mg TID, approximately 10% less than should have been given per protocol.

Subject Identifier	GP3CCF-001
Age	60
Sex	Male
Baseline Weight (kg)	92.7
Race	Caucasian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	10 Oct 2017
Event	1. Septic Shock 2. Subarachnoid Hemorrhage
Severity	1. Grade 4 2. Grade 1
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 20 Oct 2017 – 22 Oct 2017 2. 17 Feb 2018 – 19 Apr 2018
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. NA (Pre-transplant event) 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3CCF-001 is a 60-year-old Caucasian male with AML who received a Omidubicel transplant on 20-Oct-2017.

The patient was diagnosed with acute myeloid leukemia with maturation M2 on 23-Jun-2017. The patient underwent induction therapy with cytarabine and idarubicin x 2 cycles (29-Jun-2017 to 21-Jul-2017) and one course of consolidation therapy with HiDAC (24-Aug-2017 to 29-Aug-2017). Other medical history included insulin dependent diabetes, moderate pulmonary function, hypertension, hypercholesterolemia, and positive CMV treated with ganciclovir. Prior to study entry, the patient had an episode of vancomycin-resistant Enterococcus bacteremia treated with high-dose daptomycin (Jul-2017).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165cGy (16-Oct-2017 to 19-Oct-2017), fludarabine 54 mg/day (12-Oct-2017 to 14-Oct-2017), and cyclophosphamide 5676 mg/day (12-Oct-2017 to 13-Oct-2017). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included valacyclovir, ciprofloxacin, and fluconazole. Neutrophil counts recovered at 10 days post-transplantation (30-Oct-2017). The patient was discharged from the hospital on 04-Nov-2017.

The patient was initially admitted for study transplant on 20-Oct-2017. The patient was diagnosed with septic shock on 20-Oct-2017 prior to study product infusion. The patient developed a high grade fever (>39^{o}C) and hypotension (systolic pressure of 70 mmHg) in the setting of neutropenia. He did not respond to IV fluid boluses and had an elevated lactate of 6.6. His ABG showed alkalosis. His venous blood gas (VBG) showed MVO2 of 56 which was consistent with hypovolemia. The acute medical emergency team was called. The patient required pressors (norepinephrine) and was transferred to the MICU. At that time his ANC was 0. Blood cultures were drawn, and the patient was started on vancomycin and Zosyn. The patient received a single dose

of tobramycin. The patient's ciprofloxacin prophylaxis was held during the time he was receiving Zosyn. Chest x-ray showed no consolidation or infiltrates. On 22-Oct-2017, he was transferred back to the floor from the MICU and the septic shock event was considered resolved. On 23-Oct-2017, an *E. coli* infection was identified, and his hypotension was reported as resolved.

The patient was then transferred from an outside hospital on 20-Feb-2018 after a fall on 17-Feb-2018 which resulted in a small right subarachnoid hemorrhage. The patient apparently fell down 17 stairs and may have lost consciousness. He sustained a small non-displaced right clavicular fracture and a small subarachnoid hemorrhage in the right sylvian fissure. The subarachnoid hemorrhage did not require surgical intervention. In the outside hospital the patient was reportedly given oxycodone for pain and subsequently developed hypoxia, mild hypotension, and drowsiness. The patient's wife reported that the patient seemed a bit slower in thinking and at times intermittently confused since the fall.

On transfer admission the patient was on 5L nasal cannula. The hospital course was complicated by fever, hypoxia, and sputum culture positive for *E. Coli* that was treated by piperacillin/tazobactam. On 22-Feb-2018 the patient was clinically stable. On 23-Feb-2018 the patient's mental status had improved, and he was afebrile. The patient was discharged home on 24-Feb-2018. The subarachnoid hemorrhage event was considered resolved on 19-Apr-2018.

Subject Identifier	GP3CCF-002
Age	40
Sex	Female
Baseline Weight (kg)	60.2
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	08 Jun 2018
Event	1. Nausea 2. Dysarthria 3. Inferior vena cava (IVC) Thrombus 4. Clonal T-Cell Expansion
Severity	1. Grade 3 2. Grade 2 3. Grade 2 4. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 30 Jul 2018 – 14 Aug 2018 2. 12 Aug 2018 – 15 Aug 2018 3. 12 Nov 2018 – 10 Jun 2019 4. 14 Dec 2018 – 12 Jun 2020
Outcome Of Event	1. Resolved with sequelae 2. Resolved 3. Resolved by convention 4. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. Yes
Date Of Death (If Applicable)	
Narrative: Patient GP3CCF-002 is a 40 year-old White female with CML who received a Omidubicel transplant on 08-Jun-2018.	

The patient was diagnosed with CML [chronic phase with no history of blast crisis, partial cytogenetic remission (Ph+ metaphases >0% but <35%)] on 03-Oct-2016. She was initially managed with dasatinib but she lost her initial major molecular response by 12 months and had intolerance to the drug despite dose reduction. She then received bosutinib in Oct-2017 but due to intolerance to the drug, including marked elevation in her liver enzymes, diarrhea, nausea, and fatigue, and despite dose reduction, she stopped the therapy. She was reluctant to receive further TKI therapy. Her past medical history included depression, anxiety, hypertension, hyperactive bladder (self-catheterization at bedtime daily – for the prior 5 months), gastroesophageal reflux disease, dyshidrotic eczema (hands and feet), and occasional migraines. She also had a history of idiopathic thrombocytopenic purpura (ITP) diagnosed about 10 years prior which had been managed with steroids, IVIG, and splenectomy in April of 2006. The splenectomy had been within 6 months of diagnosis of ITP and the patient had been on long-term infection prophylaxis with azithromycin thereafter. Surgical history also included sinus surgery (2013), fissurectomy and pneumatic balloon dilation of anal sphincter (2013), arthroscopic surgery of the left shoulder (2010), excision of cyst of right external auditory meatus (2003), and tonsillectomy.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of totally body irradiation 165 cGy/day (04-Jun-2018 to 07-Jun-2018), fludarabine 50 mg/day (31-May-2018 to 02-Jun-2018), and cyclophosphamide 3894 mg/day (31-May-2018 to 01-Jun-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Cyclosporine was switched to tacrolimus on 20-Jul-2018. Tacrolimus was discontinued on 20-Nov-2018 since the patient was without evidence of GvHD. Neutrophil counts recovered at six days post-transplantation (14-Jun-2018). The patient was discharged from the hospital on 18-Jun-2018.

The patient was hospitalized for nausea from 30-Jul-2018 to 14-Aug-2018 (no GvHD) and for dysarthria from 12-Aug-2018 to 15-Aug-2018. Both the nausea and dysarthria events were likely secondary to high levels and secondary adverse effects of calcineurin inhibitor treatment. The patient developed CMV viremia on 03-Aug-2018 with tissue invasive gastric involvement for which she received ganciclovir and then valganciclovir. On 12-Aug-2018 the patient was noted to have lymphocytosis with an absolute lymphocyte count of 6070 that peaked at 9610 on 20-Aug-2018 and then resolved by 28-Aug-2018. She had both CMV viremia and tissue invasive disease at that time based on an EGD from 16-Aug-2018 that reported rare CMV infected cells from a stomach biopsy. The patient completed treatment with ganciclovir and valganciclovir on 01-Oct-2018. Her CMV infection cleared by 14-Sep-2018.

A post-transplant BM examination on 11-Sep-2018 showed no evidence of leukemia. Cytogenetics revealed a normal male karyotype (donor cells) 46 XY, her peripheral blood RT-PCR for p210 BCR/ABL transcripts was negative, and she had achieved complete donor chimerism (14-Sep-2018: 96%). The patient was then hospitalized with IVC thrombosis on 12-Nov-2018. She was discharged home on 14-Nov-2018 on enoxaparin twice daily.

The patient's absolute lymphocyte counts were found to be increased from 5140 on 13-Nov-2018 to 10,050 on 07-Dev-2018. She had a flow cytometric analysis performed on 14-Dec-2018 to further evaluate the lymphocytosis. It was reported that there was "no definite immunophenotypic evidence of involvement by a lymphoproliferative disorder". However, flow cytometric analysis of peripheral blood lymphocytes assessing T-cell receptor V-beta family usage showed a significant expansion of the V-beta Vb12 and Vb14 families within the CD3+ CD+4 subset. These findings provided immunophenotypic evidence of a Clonal T-Cell Expansion. T-cell clonality PCR assessment was also performed and was positive for a clonal rearrangement detected by PCR in one or more primer sets targeting the T-cell receptor beta or gamma (TCRG) chain loci. This result was consistent with the presence of a monoclonal T-cell population. Based on these findings she was diagnosed with Clonal T-Cell Expansion (14-Dec-2018). A T-cell lymphoproliferative disorder was ruled out.

The patient's lymphocyte count peaked at 11,140 on 07-Jan-2019. From Sep-2018, the patient had negative CMV DNA and EBV DNA PCR testing. On 10-Jan-2019, a skin biopsy from the patient's right upper extremity was consistent with histologic Grade 1 of 4 GvHD that subsequently resolved with topical

triamcinolone cream. Follow-up CT scans of the chest, abdomen, and pelvis on 22-Jan-2019 were negative for lymphadenopathy, masses, or acute findings.

On 04-Feb-2019, the patient's lymphocyte count was 9010. On 04-Feb-2019, a Hematologic Neoplasm Next Generation Sequencing Panel was performed. The sequencing analysis reported variants of uncertain significance in CUX1 and TET2. No data is available on the significance of the CUX1 variant, while the TET2 variant is favored to be a population variant given its presence in population databases and possibly represents a germline variant. The testing was negative for STAT3.

The Clonal T-Cell Expansion event was reported in the data system on 27-Feb-2019. The patient continued to follow-up outpatient with hematology/oncology. Her lymphocytosis remained unchanged over time. She was under observation for her lymphocytosis, including monitoring of T-cell clones every 6 months and scans as indicated clinically. Repeat CT scans of the chest, abdomen, and pelvis on 01-May-2019 were without lymphadenopathy. The Clonal T-Cell Expansion event was considered resolved on 12-Jun-2020.

The patient was seen for a follow-up visit on 17-Jun-2019. At the time she was receiving enoxaparin 60 mg twice daily (later transitioned to apixaban 5 mg twice daily) as continued treatment for the IVC thrombus. She was tolerating the treatment without bleeding or bruising side effects. Venous duplex completed prior to the follow-up showed partial recanalization with phasic flow throughout (IVC and distally) suggesting insignificant venous compression. The IVC thrombus event was considered resolved by convention on 10-Jun-2019.

Subject Identifier	GP3CCF-003
Age	59
Sex	Male
Baseline Weight (kg)	84.1
Race	White
Study Therapy	Not received
Date Of Study Therapy Administration	NA
Event	1. Relapse 2. Neutropenic Fever 3. Disease Progression
Severity	1. Grade 2 2. Grade 3 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 05 Dec 2018 – 06 Feb 2019 2. 22 Feb 2019 – 25 Feb 2019 3. 11 May 2019 – 11 May 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. NA: Pre-transplant event 3. NA
Date Of Death (If Applicable)	11 May 2019

Narrative:

Patient GP3CCF-003 is a 59-year-old White male with AML who consented to the Omidubicel GP3 study on 07-Nov-2017 and was randomized to the control arm (unmanipulated CBU). The patient did not receive the

study transplant within 90 days of randomization and was therefore enrolled in the Post-randomization Follow-Up (Limited Follow-Up) segment.

The patient was diagnosed with acute myelogenous leukemia [AML with multilineage dysplasia, FLT3 ITD+, which transformed from myelodysplastic syndrome (MDS)] on 08-Aug-2018. He underwent induction therapy with 7+3 (cytarabine and daunorubicin) starting on 14-Aug-2018. He also received midostaurin from 23-Aug-2018 to 06-Sep-2018. Salvage therapy with MEC was given on 24-Sep-2018. A repeat BM biopsy on 07-Nov-2018 showed no morphologic evidence of leukemia but a background of dysplasia. The patient's medical history included a hiatal hernia (2009) and MDS (2005).

During a regularly scheduled pre-transplant clinic visit, the patient's bloodwork revealed a decreased platelet count and 12% peripheral blasts (05-Dec-2018). Bone marrow biopsy on 07-Nov-2018 had shown 1% blasts in marrow. The patient was diagnosed with relapse of AML on 05-Dec-2018. Plans for the transplant were put on hold to start salvage therapy for disease control. The patient was given azacitadine and sorafenib (later changed to gilteritinib) starting on 12-Dec-2018. A BM biopsy was done on 06-Feb-2019 which was a suboptimal specimen but showed 4% blasts confirming CR2. Given that his counts were not expected to improve much more, the decision was made to proceed to a double cord transplant following a conditioning regimen consisting of fludarabine, cyclophosphamide, and TBI.

The patient was admitted on 22-Feb-2019 due to fever at home with a near-syncopal episode, as well as bilateral knee edema with pain. A CT scan revealed a left lower lobe pneumonia. A biopsy was performed on his knee which showed hemorrhage and low likelihood for leukemia cells. The patient was started on prednisone as treatment from 22-Feb-2019 to 25-Feb-2019 with a taper that started on 26-Feb-2019. Piperacillin/tazobactam (Zosyn) was also given from 22-Feb-2019 to 25-Feb-2019 for the pneumonia which was transitioned to oral levofloxacin (treatment dose) upon discharge on 25-Feb-2019.

The patient was then admitted to begin his conditioning regimen on 06-Mar-2019. He was noted to have relapsed disease which made him ineligible to proceed with the study transplant. Gilteritinib was initiated on 23-Mar-2019. The patient experienced an episode of shortness of breath with hypoxia which prompted a transfer to the ICU on 25-Mar-2019 but he recovered and was discharged home on 04-Apr-2019.

The patient continued to be followed regularly but remained profoundly pancytopenic and deconditioned. His disease was determined to be refractory on 29-Apr-2019 and due to limited treatment options and worsening organ function, the patient enrolled in hospice. The patient's death on 11-May-2019 was discovered through an obituary search. The site investigator reported the primary cause of death as disease progression.

Deviations with potential medical significance: Protocol-specified BM flow cytometry at screening (within 3 weeks prior to randomization for AML patients) was ordered but was cancelled by the performing lab as "not necessary". A peripheral blood sample was obtained, and flow cytometry was performed on this sample, in lieu of BM. In addition, the patient had molecular changes at diagnosis (FLT3+). No molecular marker testing was performed during the screening period.

Subject Identifier	GP3CCF-004
Age	51
Sex	Male
Baseline Weight (kg)	59.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	21 Dec 2018
Event	1. Generalized Weakness 2. Hypoxia 3. Right-sided Chest Wall Pain 4. Acute Hypoxemic Respiratory Failure
Severity	1. Grade 3

	2. Grade 3 3. Grade 3 4. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 06 Mar 2019 – 09 Mar 2019 2. 25 Mar 2019 – 3 Apr 2019 3. 18 May 2019 – 21 Jun 2019 4. 28 May 2019 - 21 Jun 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Death 4. Death
Relationship To The Study Drug	1. No 2. No 3. No 4. No
Date Of Death (If Applicable)	21 Jun 2019

Narrative:
Patient GP3CCF-004 is a 51 year-old White male with AML who received an Unmanipulated CBU transplant on 21-Dec-2018.

The patient was diagnosed with AML (with multilineage dysplasia) on 30-Jul-2018. He underwent therapy with 7+3 induction, HiDAC consolidation, and Midostaurin. His past medical history at screening included mild hepatic impairment (AST 52) and severe pulmonary dysfunction (cDLCO 63% on 21-Nov-2018). Surgical history included appendectomy. He had allergies to penicillin and iodine contrast.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (17-Dec-2018 to 20-Dec-2018), fludarabine 51 mg/day (13-Dec-2018 to 15-Dec-2018), and cyclophosphamide 5166 mg/day (13-Dec-2018 to 14-Dec-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Neutrophil counts recovered at 27 days post-transplantation (17-Jan-2019). The patient was discharged from the hospital on 28-Feb-2019. The post-transplantation period was complicated by HHV6 infection, GvHD of GI/liver/skin, and thrombotic microangiopathy.

The patient was admitted through the ED on 18-May-2019 with right-sided chest pain, low platelets (16 K/uL), elevated NT Pro BNP (777 pg/mL), troponin leak, and chest x-ray concerning for pulmonary edema. CT chest showed mild diffuse interlobular septal thickening. The patient's chest pain improved with morphine. EKG, troponin, and CK-MB were all negative. Cardiac causes were ruled out and he was admitted to the BMT service.

On 19-May-2019, the Adult Medical Emergency Team (AMET) was activated. The patient had a heart rate of 160, elevated lactate with rigors in the setting of fever, and urine culture positive for *Enterobacter cloacae*. The patient was treated with piperacillin-tazobactam (18-May-2019 to 27-May-2019) and transitioned to ciprofloxacin on 27-May-2019. The patient continued to have fevers, alkaline phosphatase was elevated, and right upper quadrant (RUQ) ultrasound was positive for sludge (no ductal dilation or cholecystitis was noted). He had episodes of diarrhea, but *C. diff* PCR was negative. On 28-May-2019, the patient began to desaturate requiring 5L via nasal cannula. The patient's oxygen needs continued to escalate to 50% venturi mask. The patient was transferred on 28-May-2019 to the MICU on 100% non-rebreather mask for management of acute hypoxemic respiratory failure.

CT chest on 29-May-2019 showed progressive ground-glass opacities and dense peripheral consolidations concerning for pulmonary edema vs infection vs hemorrhage. The patient was intubated on 30-May-2019 and a bronchoscopy was done. The results were negative for histology, legionella, and streptococcus Group B. He was continued on antimicrobials. On 30-May-2019 the patient had a low grade fever but was hemodynamically

stable. He was then taken off pressors on 31-May-2019. On a Pressure Support ventilation trial 8/5, he did well in the test of tidal volume (VT), but appeared to be working hard to breathe. His respiratory rate was in the 30s. On 01-Jun-2019 he required approximately 3 hours of norepinephrine (Levophed). He was then hemodynamically stable. The patient's hemoglobin was noted to have dropped from 7.8 to 6.5 g/dL, with a repeat of 6.7 g/dL, so one packed red blood cell transfusion was given. The patient was extubated on 01-Jun-2019 and started on 60% high-flow face mask. He refused to be placed on BiPAP. Chest x-ray showed no changes.

The patient was then able to tolerate BiPAP overnight with 8/4 settings. Meanwhile, cultures remained negative. The MICU team spoke with the BMT regarding adding an anti-TNF (etanercept) vs. high-dose steroids given the possibility of severe inflammation stemming from GvHD. He was tolerating BiPAP at 55%, however desaturated to the 70s when the mask was removed to give medications. Respiratory viral panel was ordered, and Hepatitis panel was negative. On 03-Jun-2019 the patient had decompensating respiratory status and he was started on solumedrol 1000 mg IV (03-Jun-2019 to 07-Jun-2019). The patient completed piperacillin-tazobactam on 05-Jun-2019. Fluticasone, azithromycin, and montelukast were started for five days on 05-Jun-2019. The patient was transferred out of the MICU on 08-Jun-2019 due to improvement in respiratory status [4 L nasal cannula (NC)].

On 09-Jun-2019, the patient began to desaturate to 70-80s and required MICU re-admission with high-flow NC. ABG was 7.47/47.3/83 on 6 L NC. CT chest on 10-Jun-2019 showed ground-glass opacities, moderate pneumomediastinum, and small left-sided pneumothorax. Blood cultures and doppler were negative. The patient remained hemodynamically stable at 5-6 L NC.

Despite imaging, cultures, and bronchoscopy, the etiology of respiratory failure was unknown, and the patient did not respond to empiric trials. His family ultimately chose to enroll him in hospice. He was transitioned to DNR-CC and transferred to hospice on 21-Jun-2019.

The patient had agonal breathing at the time of admission to hospice and his fentanyl infusion was increased to achieve comfort. He remained on high-flow oxygen and comfort medications were made available. He passed away on 21-Jun-2019. Primary cause of death was noted as hypoxic respiratory failure, with secondary causes of death noted as inflammatory lung disease and AML. Autopsy was not done.

Deviations with potential medical significance: Treatment CBU #1 was infused as a single Unmanipulated CBU infusion. However, this 4/6 HLA-matched unit only had a total nucleated cell dose of 3.4 x 10e7 cells/kg and a total CD34+ dose of 1.4 x 10e5 cells/kg. Per section 7.1 of the protocol, a second unit should have been infused as the total nucleated cell and CD34+ cell doses were below the allowable threshold for a single CBU with a 4/6 HLA match score.

Subject Identifier	GP3CCF-005
Age	50
Sex	Male
Baseline Weight (kg)	70.9
Race	White
Study Therapy	Not received
Date Of Study Therapy Administration	NA
Event	1. Relapse 2. Near Syncope 3. Relapse
Severity	1. Grade 3 2. Grade 2 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes

Start/stop date of Event	1. 20 Feb 2019 – 10 Apr 2019 2. 26 Apr 2019 – 09 May 2019 3. 22 Apr 2019 – 26 Nov 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. NA: Pre-transplant event 3. NA: Pre-transplant event
Date Of Death (If Applicable)	26 Nov 2019

Narrative:
Patient GP3CCF-005 is a 50 year-old White male with AML who consented to participate in the Omidubicel GP3 study on 28-Jan-2019, was randomized on 08-Feb-2019, and was scheduled for study transplant admission on 20-Feb-2019. The patient did not receive the study transplant due to disease relapse during the transplant admission.

The patient was diagnosed with acute myelogenous leukemia (multilineage dysplasia, FLT3 ITD+ AML) on 18-Oct-2018. He underwent induction therapy with 7+3 (cytarabine and daunorubicin) starting on 19-Oct-2018. He also received midostaurin from 27-Oct-2018 to 09-Nov-2018. A repeat BM biopsy on 01-Nov-2018 was hypocellular (5-10%) however an additional BM biopsy on 08-Nov-2018 was negative for disease and confirmed CR1. The patient received consolidation therapy with HiDAC. Cycle 1 started on 26-Nov-2018 and cycle 2 started on 02-Jan-2019. The patient's medical history included hypertension, restless leg syndrome, pancytopenia due to chemotherapy, and a hernia. The patient had reported allergies to fentanyl and sulfa drugs.

The patient was admitted on 20-Feb-2019 with plans to undergo a study transplant. As part of the workup, blood counts were drawn on 21-Feb-2019 which found 23% circulating blasts. The patient was transferred to the leukemia service for further management. He underwent a BM biopsy on 22-Feb-2019 and was discharged home that same day. He was readmitted on 25-Feb-2019 to begin reinduction therapy and was enrolled in a clinical trial. He received five doses of hydroxyurea (25-Feb-2019 and 26-Feb-2019) and then started treatment with alvocidib, cytarabine, and mitoxantrone. A BM biopsy done on 10-Apr-2019 showed no morphologic evidence of disease. Blood counts done at a local lab on 22-Apr-2019 showed 8% blasts.

During an outpatient clinic visit on 26-Apr-2019 for evaluation of AKI, the patient had multiple sets of orthostatic vital signs and became lightheaded/dizzy after transitioning from sitting to standing. The patient was also hypotensive and tachycardic. The Medical Emergency Response Team was activated, and the patient was transported to the ED and then admitted to the hospital for evaluation of syncope. The patient's symptoms improved with intravenous (IV) fluids and transfusions. Discharge was delayed due to another episode of lightheadedness and dizziness which improved with IV fluids and transfusions. The patient subsequently had fevers and was started on IV antibiotics. Blood cultures were negative.

Blood counts drawn on 02-May-2019 revealed 49% peripheral blasts. The patient had leukocytosis due to relapsed leukemia and was started on hydroxyurea. Blood cultures were negative and since the fevers were likely secondary to leukemia, the IV antibiotics were discontinued. Treatment was started with seven days of azacytidine on 03-May-2019. The patient was discharged home on 09-May-2019 and was started on gilteritinib. A baseline EKG obtained on the day of discharge showed a QTc of 440 ms for which the patient was instructed to follow up with his physician.

A BM biopsy on 07-Jun-2019 showed 3% blasts. Gilteritinib was stopped on 26-Jun-2019 in anticipation of BMT. Repeat BM biopsy on 01-Jul-2019 showed 12% blasts. It was recommended that the patient continue with a second cycle of azacytidine with gilteritinib (10-Jul-2019 to 16-Jul-2019). The patient was noted to have persistent disease after cycle 2. Azacytidine was continued, with ivosidenib added on 09-Nov-2019.

The patient began to show signs of clinical decline with increased fatigue and anorexia on 13-Nov-2019 and was admitted on 14-Nov-2019. An MRI of the brain suggested intracranial/CSF involvement of AML with

leptomeningeal carcinomatosis, and periventricular and cortical/subcortical parenchymal disease. No acute stroke or intracranial hemorrhage was noted. The patient was started on dexamethasone. Given the current state of his disease, the patient elected to transition to hospice on 16-Nov-2019. The patient expired on 26-Nov-2019. The primary cause of death was noted as disease relapse. An autopsy was not done.

Subject identifier	GP3CCF-006
Age	26
Sex	Male
Baseline weight (kg)	74.3
Race	Black, African-American
Study therapy	Omidubicel
Date of study therapy administration	04 May 2019
Event	1. Fever 2. Seizure 3. Relapsed AML 4. GvHD of the Gut – Grade 4 5. Dehydration 6. Abdominal Pain 7. Bilateral Lower Extremity Edema 8. Right Femoral Neck Fracture 9. Chronic Active Gastritis 10. Fever
Severity	1. Grade 3 2. Grade 2 3. Grade 3 4. Grade 3 5. Grade 3 6. Grade 2 7. Grade 1 8. Grade 3 9. Grade 2 10. Grade1
Serious (yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes 6. Yes 7. Yes 8. Yes 9. Yes 10. Yes
Start/stop date of Event	1. 19 Feb 2019 – 21 Feb 2019 2. 29 Apr 2019 – 29 Apr 2019 3. 25 Feb 2019 – 18 Mar 2019 4. 18 Jun 2019 – 20 Sep 2019 5. 30 Sep 2019 – 02 Oct 2019 6. 12 Jan 2020 – 17 Jan 2020 7. 25 Jan 2020 – 26 Feb 2020 8. 16 Apr 2020 – 21 Apr 2020 9. 22 Apr 2020 – 01 May 2020 10. 26 May 2020 – 29 May 2020
Outcome of event	1. Resolved 2. Resolved

	3. Resolved 4. Persistent condition 5. Resolved 6. Resolved 7. Resolved with sequelae 8. Resolved 9. Resolved 10. Resolved
Relationship to the study drug	1. NA: Pre-transplant event 2. NA: Pre-transplant event 3. NA: Pre-transplant event 4. Yes 5. No 6. No 7. No 8. No 9. No 10. No
Date of death (if applicable)	15 Sep 2020

Narrative:
Participant GP3CCF-006 is a 26 year-old Black, African-American male with Acute Myelogenous Leukemia who received an omidubicel transplant on 04-May-2019.

The participant was diagnosed with Acute Myelogenous Leukemia [AML with t(8:21)(q22;q22)] on 16-Jan-2018. He underwent the first cycle of induction with cytarabine, daunorubicin, and etoposide from 18-Jan-2018 to 25-Feb-2018. The second cycle of induction was given from 26-Feb-2018 to 25-Mar-2018 with cytarabine, daunorubicin, etoposide, and mylotarg. Two cycles of intensification with cytarabine and etoposide were given from 26-Mar-2018 to 26-Jun-2018. His disease relapsed on 27-Feb-2019 and reinduction therapy with idarubicin, cytarabine, fludarabine, dexrazoxane, and allopurinol was started on 28-Feb-2019. The participant's past medical history included psychiatric disturbance (previous, not present at screening). He had mild hepatic, moderate/severe renal, and severe pulmonary impairment at study screening. The participant's surgical history included a renal biopsy and femoral neck fixation. He had reported allergies to platelets and pentamidine.

Prior to transplant admission, the participant presented to the Emergency Department (ED) on 19-Feb-2019 with a fever but was otherwise clinically stable. Given his immunocompromised state and the presence of a central line, he received vancomycin and piperacillin/tazobactam and was admitted for further workup and treatment. Flu test, blood cultures, and urine culture were all negative. Creatinine was found to be elevated. This was considered to be likely related to the antibiotics and discontinuation of intravenous fluids. Fluids were then restarted and participant's creatinine level down trended to 1.78 mg/dL prior to discharge. The participant was discharged on 21-Feb-2019.

Prior to the omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine 36.4 mg/day (25-Apr-2019 to 27-Apr-2019), cyclophosphamide 4206 mg/day (25-Apr-2019 to 26-Apr-2019), and total body irradiation (TBI) 164 cGy/day (29-Apr-2019 to 03-May-2019). During the first dose of TBI on 25-Apr-2019, the participant was noted to have an episode of seizure-like activity. Neurology reported the symptoms were consistent with syncopal convulsion. An MRI of the brain was negative for any acute process. The participant recovered the same day without any intervention.

GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Neutrophil counts recovered at seven days post-transplantation (11-May-2019). The participant was discharged from the hospital on 10-Jun-2019. The post-transplant course was complicated by thrombotic microangiopathy, chronic kidney disease, and COVID-19.

The participant was seen in clinic on 18-Jun-2019 and his cyclosporine level was noted to be > 500 ng/mL. He was noted to have a flat affect, refusal to eat or drink, and an increase in stool output. Therefore, the participant

was admitted for evaluation and monitoring of GvHD vs *Clostridium difficile* colitis. *C. difficile* was found to be positive on 21-Jun-2019, and the participant was started on oral metronidazole. Cyclosporine was withheld on admission and repeat levels were < 200 ng/mL. Cyclosporine was restarted at a decreased dose on 23-Jun-2019. Prednisone was weaned on 24-Jun-2019.

On 25-Jun-2019, the participant was noted to have an erythematous rash over 16% of his body (stage 1 skin), 1450 mL of diarrhea (stage 2 lower GI), and persistent nausea, vomiting, and/or anorexia (stage 1 upper GI). Methylprednisone was started the following day. Over the course of the admission, a CT scan and EGD confirmed the presence of GvHD which was classified as steroid-refractory. The participant was treated with vedolizumab, infliximab, ruxolitinib, and tacrolimus. He continued to receive treatment for the *C. difficile* as well as GvHD and was discharged on 20-Sep-2019.

The participant was admitted on 30-Sep-2019 for management of dehydration due to increased stool output, abdominal pain, and decreased appetite over the past week which was thought to be a possible flare of the acute GvHD. The participant received IV fluids, stress dose steroids, and vedolizumab. He was discharged on 02-Oct-2019 after 24 hours of no diarrhea.

The participant started having abdominal pain around 06-Jan-2020 which worsened over the week to include diarrhea and occasional vomiting despite receiving fluids, pain medication, and steroids. He was admitted on 12-Jan-2020 for pain and nausea management. Pain was reported to be constant and not localized to a specific area. The participant was started on hydromorphone on 10-Jan-2020 and he had no diarrhea thereafter. His appetite and fluid intake were decreased and his previously reported right hip pain had worsened. The participant continued receiving treatment with pain medications, tacrolimus, and ruxolitinib. A colonoscopy was performed on 15-Jan-2020 which was concerning for GvHD. Prednisone and budesonide were started with a plan to administer vedolizumab as an outpatient on 20-Jan-2020. He was discharged on 17-Jan-2020.

The participant was seen in clinic on 24-Jan-2020 where he received IV fluids. Later that evening he noticed some swelling of his knees and ankle. The participant woke up with difficulty walking on 25-Jan-2020 due to the increased swelling. He was admitted for further work up and management of the edema, weight gain, and increased pain. The leg swelling improved with furosemide and a low sodium diet. Most of the pain was in his right hip due to previously existing avascular necrosis after an old injury. The pain was attempted to be managed with IV hydromorphone. An orthopedic surgery consult was held on 31-Jan-2020 and no acute orthopedic intervention was taken at that time as the pain was thought to be from the edema/myositis. The participant was referred for an arthrotomy and underwent hardware removal, irrigation, and debridement of his right hip on 07-Feb-2020. He was discharged on 26-Feb-2020.

The participant was then admitted on 16-Apr-2020 for a planned surgery for a right femoral neck fracture in the setting of the recent hip hardware removal. He underwent the procedure on 17-Apr-2020. The postoperative course was unremarkable, and the participant's pain was well controlled. He was discharged to home on 21-Apr-2020.

The participant was admitted again on 22-Apr-2020 for complaints of non-radiating, midsternal/epigastric pain and dizziness. He underwent an EGD which revealed *Candida galbrata*. Micafungin was initiated for treatment. He was discharged on 01-May-2020.

The participant was admitted on 26-May-2020 with a one to two-day history of fevers, vomiting, and decreased oral intake. Due to the history of GvHD and esophagitis, the participant underwent an upper GI scope as well as a sigmoidoscopy. The procedures failed to show any evidence of infection or GvHD. He was discharged on 29-May-2020.

The participant died on 15-Sep-2020 due to viral encephalitis.

Subject Identifier	GP3CCF-007
Age	44

Sex	Male
Baseline Weight (kg)	97.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	01 Nov 2019
Event	1. Relapsed AML 2. Worsening Heart Failure 3. IPS
Severity	1. Grade 3 2. Grade 3 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 10 Jun 2019 – 01 Oct 2019 2. 21 Nov 2019 – 28 Dec 2019 3. 08 Dec 2019 – 28 Dec 2019
Outcome Of Event	1. Resolved 2. Death 3. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. No 3. No
Date Of Death (If Applicable)	28 Dec 2019

Narrative:
Patient GP3CCF-007 is a 44 year-old White male with AML who received an Unmanipulated CBU transplant on 01-Nov-2019.

The patient was diagnosed with AML (with monocytic differentiation) on 16-Jan-2019. He underwent induction therapy with 7+3 with idarubicin from 16-Jan-2019 to 19-Jan-2019 and cytarabine from 16-Jan-2019 to 23-Jan-2019. One cycle of HiDAC consolidation was given on 21-Mar-2019. CNS was negative for disease involvement. The patient received prophylactic intrathecal methotrexate. Routine lab work performed on 10-Jun-2019 was suspicious for disease relapse due to an elevated WBC count (24.26 k/uL) with 70% blasts. Bone marrow exam on 13-Jun-2019 confirmed disease relapse. Treatment included hydroxyurea from 14-Jun-2019 to 18-Jun-2019 followed by treatment with CPX-351 and palbociclib. The patient underwent a BM exam on 03-Jul-2019 (day 14) which showed no evidence of leukemia. On 05-Aug-2019, the patient's disease relapsed again. He received further treatment with another clinical trial consisting of MEC +/- uproleselan (GMI). A third complete remission was achieved on 01-Oct-2019. The patient received a short course of gilteritinib prior to admission for the cord blood transplant. The patient's past medical history included non-ST-elevation myocardial infarction, depression, unspecified skin cancer, and testicular cancer. He had moderate pulmonary dysfunction (cDLCO 70%) at study screening. Surgical history included an appendectomy and ankle fracture repair.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 56 mg/day (24-Oct-2019 to 26-Oct-2019), cyclophosphamide 5874 mg/day (24-Oct-2019 to 25-Oct-2019), and TBI 165 cGy/day (28-Oct-2019 to 31-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Neutrophil counts recovered at 40 days post-transplantation (11-Dec-2019).

On 21-Nov-2019, the AMET was activated. The patient had a respiratory rate of 32, oxygen saturation of 98% on 50% venti-mask, heart rate of 96 bpm, and elevated blood pressure of 148/109. The patient was transferred to the MICU for tachypnea and hypoxemia related to fluid overload. The patient was treated with aggressive diuresis and weaned off noninvasive ventilation. Antibiotics were continued. An echocardiogram on 24-Nov-2019 showed a decreased ejection fraction (26% down from 51% on 01-Oct-2019) and no valvular abnormalities. Over the next two days, the supplemental oxygen continued to be weaned and diuresis with

furosemide continued resulting in 2.8 L of urine output overnight. The Cardiology service was consulted on 25-Nov-2019 due to the patient's decreased ejection fraction and respiratory compromise. The recommendation was to continue metoprolol succinate, furosemide, and lower the dose of lisinopril for the chemotherapy-induced cardiomyopathy. The aggressive diuresis led to an AKI with worsening serum creatinine (1.4 mg/dL). The patient was transferred back to the transplant unit on 27-Nov-2019.

The patient remained in the transplant unit with intermittent confusion and persistent neutropenia. A chest x-ray and chest CT scan on 07-Dec-2019 showed bilateral opacities concerning for pulmonary edema and/or an infectious process. On 08-Dec-2019, the patient was febrile (38.2ºC) with increased work of breathing and confusion. Lab work showed a hemoglobin of 5.8 mg/dL (previously 7.5 mg/dL) and a platelet count of 6 $\times 10^9$/L. The patient developed an acute increase in oxygen requirement via nasal cannula (from 5% to 12%) to maintain oxygen saturations at 95%. AMET was called to the bedside. ABG results were consistent with hypoxic respiratory failure. A venti-mask was applied, and the patient was transferred to the MICU. The supplemental oxygen was escalated to a non-rebreather mask and ultimately BiPAP for improved oxygenation.

The hypoxia was thought to be related to fluid overload and anemia, so treatment with aggressive diuresis and blood product transfusions was initiated. On 10-Dec-2019, a feeding tube was placed due to the possibility of aspiration. A bronchoalveolar lavage was also performed. After the procedure, the patient's oxygen requirements increased throughout the day with desaturations with movement or coughing. The patient was subsequently intubated. He developed severe distributive shock following intubation. The patient was given daptomycin for a history of vancomycin-resistant enterococci infection (VRE), amikacin, and stress steroids. After showing signs of clinical improvement, the patient was electively extubated on 16-Dec-2019. The patient was reintubated on the afternoon of 17-Dec-2019 after an episode of suspected aspiration of emesis and worsening work of breathing. A bronchoscopy was performed on 18-Dec-2019 which showed clear lungs.

The patient was subsequently placed on CVVH on 21-Dec-2019. A pneumomediastinum was found on CT scan on 26-Dec-2019 and thought to be secondary to barotrauma. Despite adequate diuresis, empiric infection treatment, and steroids for possible diffuse alveolar hemorrhage, a decision was made by the family to palliatively extubate on 28-Dec-2019. The patient expired later that afternoon secondary to respiratory failure most consistent with IPS. An autopsy was not performed.

Deviations with potential medical significance: Alkaline phosphatase, AST, and ALT were not assessed as part of the serum chemistry results at day +42 post-transplant.

Subject Identifier	GP3CHC-001
Age	28
Sex	Female
Baseline Weight (kg)	56.0
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	16 Nov 2018
Event	Food Poisoning
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	10 Feb 2019 – 14 Feb 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	
Narrative: Patient GP3CHC-001 is a 28 year-old White female with AML who received an Unmanipulated CBU transplant on 16-Nov-2018. The patient was diagnosed with AML on 07-Jun-2018. She underwent induction with one cycle of cytarabine standard 7+3 with Idarubicin starting on 12-Jun-2018 and consolidation with HiDAC and midostaurin starting	

01-Aug-2018. The patient's past medical history included cerebrovascular disease that was absent at study screening and moderate pulmonary impairment that was present at study screening (DLCO = 73%, cDLCO = 74%).

Prior to UCB transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (12-Nov-2018 to 15-Nov-2018), fludarabine (09-Nov-2019 to 11-Nov-2018), and cyclophosphamide (09-Nov-2018 to 10-Nov-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included trimethoprim-sulfamethoxazole, levofloxacin, micafungin, and acyclovir. Neutrophil counts recovered at 17 days post-transplantation (03-Dec-2018). The patient was discharged from the hospital on 19-Dec-2018.

The patient presented on 10-Feb-2019 with intractable nausea and vomiting and was admitted for further assessment. She reported eating fairly well on 09-Feb-2019 and then waking up to multiple episodes of vomiting on 10-Feb-2019. She denied any febrile episodes or sick contacts but did admit to eating out and was not sure if this related to her presentation. The patient improved overnight and endorsed only intermittent nausea and the cessation of vomiting. She had three loose stools on 13-Feb-2019 that resolved. The patient was discharged on 14-Feb-2019 at which point her appetite had improved.

Subject Identifier	GP3CHC-004
Age	45
Sex	Female
Baseline Weight (kg)	58.6
Race	Asian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	21 Jun 2019
Event	1. CMV Viremia 2. Skin GvHD 3. Septicemia due to Catheter 4. Traumatic Subarachnoid Hemorrhage 5. Altered Mental Status
Severity	1. Grade 3 2. Grade 2 3. Grade 3 4. Grade 3 5. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 09 Aug 2019 – 25 Sep 2019 2. 21 Sep 2019 – 21 Oct 2019 3. 30 Oct 2019 – 05 Nov 2019 4. 03 Dec 2019 – 10 Dec 2019 5. 10 Nov 2019 – 12 Nov 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved with sequelae 5. Resolved with sequelae
Relationship To The Study Drug	1. No 2. Yes 3. No 4. No

5. No
Date Of Death (If Applicable)
Narrative: Patient GP3CHC-004 is a 45-year-old Asian female with ALL who received a Omidubicel transplant on 21-Jun-2019. The patient was diagnosed with pre-B-Cell ALL on 11-Sep-2018. Her disease was positive for the BCR-ABL1 t(9;22) translocation. She underwent induction therapy with the hyper-CVAD regimen and did not receive consolidation or maintenance therapy. The patient's past medical history included CML with lymphoblastic transformation. She had moderate pulmonary impairment at study screening. The patient had reported allergies to sulfa antibiotics and acetaminophen. Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (14-Jun-2019 to 16-Jun-2019), cyclophosphamide (14-Jun-2019 to 15-Jun-2019), and TBI (17-Jun-2019 to 20-Jun-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, atovaquone, levofloxacin, vancomycin, micafungin, and valgancyclovir. Neutrophil counts recovered at eight days post-transplantation (29-Jun-2019). The patient was discharged from the hospital on 23-Jun-2019. The patient was admitted on 09-Aug-2019 for CMV reactivation and worsening viremia (70,000 copies/mL). She was treated with intravenous (IV) foscarnet. CMV viral load increased to a maximum of 255,000 copies/mL on 19-Aug-2019. During the admission for CMV, the patient was noted to have Grade 1 skin GvHD with a scant maculopapular rash throughout the upper extremities and upper chest. The patient also had possible upper GI GvHD with mild nausea and occasional epigastric discomfort. On 21-Sep-2019, prednisone and sirolimus were initiated, and beclomethasone and mycophenolate dosages were increased. CMV viral load continued to down trend with treatment and the patient was discharged on 25-Sep-2019. Foscarnet therapy was completed on 04-Oct-2019. The patient was admitted for observation and IV therapy on 04-Oct-2019 due to fever, hypokalemia, and thrombocytopenia. Levofloxacin was started for antibiotic coverage and hydrocortisone cream was added for the rash. Electrolytes corrected with treatment and the patient was discharged on 08-Oct-2019 with close outpatient monitoring. GvHD was noted to be inactive on 12-Nov-2019. The patient was readmitted on 30-Oct-2019 for central line catheter malfunction, septicemia, and cellulitis. Treatment included vancomycin and piperacillin/tazobactam. On 31-Oct-2019, the patient experienced an episode of acute obtundation with gaze palsy and shaking. This improved with a dose of intravenous lorazepam. An MRI of the brain and CT of the facial bones were obtained and showed no acute changes. Neurosurgery was consulted and determined the event to be a seizure. The patient was started on levetiracetam and discharged home in stable condition later the same day. On 10-Nov-2019, the patient was brought to the ED after family members noticed an episode of upper body shaking followed by a period of unresponsiveness. A dose of intravenous levetiracetam was given and the patient remained lethargic. The patient was admitted for monitoring and consultation by neurology. It was determined that the patient was not taking her prescribed levetiracetam, so neurology restarted her dose at 500 mg twice a day. There were no signs or symptoms of infection. The MRI of the brain and facial CT from the prior admission were reviewed and no new imaging was recommended. The patient was back to mental status baseline, clinically improved, and medically stable for discharge on 12-Nov-2019. The patient suffered a fall at home on 03-Dec-2019 and landed on her right knee and face. She denied loss of consciousness or changes in vision. The patient was brought to the ED for evaluation. A CT of the head was negative for abnormalities. A bruise was noted on her right knee. The patient was discharged home from the ED in stable condition. On 06-Dec-2019, the patient experienced an episode of extreme anxiety, racing thoughts, and a fixation on keeping things clean. To calm her racing thoughts, the patient took both hydrocodone and lorazepam so that she could sleep. When the patient was unable to calm down, she called emergency medical services (EMS).

Upon evaluation in the ED, she denied suicidal ideation or homicidal ideation. During the assessment, the patient required a lot of redirection as she was distracted by the need to clean the room. She was unable to understand why she was in the ED. A CT of the head was obtained which showed bilateral acute subarachnoid hemorrhages with a small acute subdural hemorrhage in the right frontal and right temporal regions. The patient was admitted to the hospital for observation. Levetiracetam was discontinued and phenytoin was started with a loading dose given. The patient remained on phenytoin and was discharged on 10-Dec-2019 in stable condition.

Subject Identifier	GP3CHC-005
Age	17
Sex	Male
Baseline Weight (kg)	65.5
Race	Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	18 Oct 2019
Event	1. Septic Shock 2. ARDS
Severity	1. Grade 4 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 25 Oct 2019 – 01 Dec 2019 2. 12 Nov 2019 – 01 Dec 2019
Outcome Of Event	1. Death 2. Death
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	01 Dec 2019

Narrative:
Patient GP3CHC-005 is a 17 year-old Asian male with ALL who received an Unmanipulated CBU transplant on 18-Oct-2019.

The patient was diagnosed with ALL (pre-B-ALL, Philadelphia chromosome positive) on 29-Jun-2015. The patient was treated with standard and augmented BFM regimen backbone with imatinib. A BM biopsy and aspiration on 03-Jul-2019 confirmed relapse, without CNS involvement. Reduction was started per AALL1331 with the addition of daily dasatinib on 08-Jul-2019. A follow-up BM exam on 05-Aug-2019 suggested morphological remission and flow cytometry showed no evidence of residual disease. Consolidation therapy was started with blinatumomab on 15-Aug-2019 and cycle number one was completed on 12-Sep-2019. Cycle two was administered on 24-Sep-2019. The patient's medical history at screening included mild hepatic impairment (AST > ULN) and moderate pulmonary dysfunction (FEV1 73% on 20-Sep-2019). He had a reported allergy to trimethoprim/sulfamethoxazole.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 43 mg/day (10-Oct-2019 to 12-Oct-2019), cyclophosphamide 4020 mg/day (10-Oct-2019 to 11-Oct-2019), and TBI 165 cGy/day (14-Oct-2019 to 17-Oct-2019). Mycophenolate mofetil and tacrolimus were given as GvHD prophylaxis. Infection prophylaxis included acyclovir, atovaquone, levofloxacin, and micafungin. Neutrophil counts recovered at 29 days post-transplantation (16-Nov-2019). The post-transplantation period was complicated by HHV6 infection and bacteremia.

The patient was transferred to the ICU on 24-Oct-2019 for management of *Streptococcus viridans* sepsis and was started on antibiotics. The patient was briefly treated with dopamine and intravenous (IV) fluids for hypotension on 25-Oct-2019. He was also given a single dose of 100 mg hydrocortisone. The patient had a productive cough and was on 4 L of oxygen via nasal cannula. A chest x-ray on 27-Oct-2019 showed a new right lower lobe infiltrate. CT scan on the same day showed a diffuse intrapulmonary process. Bronchoscopy

was done on 28-Oct-2019 and the respiratory panel was negative. All cultures and PCRs were negative, however, a few rare, isolated yeast spores without hyphae were seen on bronchoalveolar lavage (BAL). Fungal studies were negative. No blood was seen during bronchoscopy and diffuse alveolar hemorrhage (DAH) was ruled out. Steroids were then weaned. Stool was also negative for *Clostridium difficile* at three time points.

The patient's condition continued to worsen from 08-Nov-2019 to 12-Nov-2019 with fevers, increased WBC count, and increased tachypnea with hypoxia. Chest x-ray showed bilateral infiltrates. Care was advanced from high-flow nasal cannula with increasing oxygen to intubation on 14-Nov-2019 due to respiratory failure. The patient also underwent BAL and transbronchial biopsy. After the BAL procedure, the patient developed ARDS. The patient's lung function worsened from 14-Nov-2019 to 20-Nov-2019 despite negative cultures. He required neuromuscular blockade for worsening hypoxemia. A decision was made to treat for idiopathic pneumonia syndrome (IPS) with steroids and etanercept.

The patient was transferred to a different facility on 21-Nov-2019 for higher level of care as the patient was in refractory hypoxemic respiratory failure. He was on maximal oxygen and high settings on the ventilator (positive inspiratory pressure of 35). The patient died on 02-Dec-2019 due to his lung condition. Primary cause of death was noted as organ failure, pulmonary. An autopsy was not done.

Subject Identifier	GP3CHC-007
Age	39
Sex	Female
Baseline Weight (kg)	108.4
Race	African American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	28 Feb 2020
Event	1. Acute GI GvHD 2. Diffuse Alveolar Hemorrhage
Severity	1. Grade 3 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 29 Mar 2020 – 14 Apr 2020 2. 19 Apr 2020 – 10 Jun 2020
Outcome Of Event	1. Resolved with sequelae 2. Death
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	10 Jun 2020

Narrative:
Patient GP3CHC-007 is a 39 year-old African American female with Acute Myelomonocytic Leukemia who received an omidubicel transplant on 28-Feb-2020.

The patient was diagnosed with Acute Myelomonocytic Leukemia (M4) on 10-Oct-2019. She underwent induction therapy with cytarabine, idarubicin, and the investigational agent crenolanib. She did not receive consolidation or maintenance therapy. The patient's past medical history included obesity. She had moderate/severe hepatic impairment (ALT elevated) at study screening. The patient had a reported allergy to dressing adhesives and chlorhexidine.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (21-Feb-2020 to 22-Feb-2020), cyclophosphamide (21-Feb-2020 to 22-Feb-2020), and TBI (24-Feb-2020 to 27-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, trimethoprim/sulfamethoxazole, levofloxacin, letermovir, micafungin, atovaquone, cefepime, and posaconazole. Neutrophil counts recovered at ten days post-transplantation (09-Mar-2020). The patient was discharged from the hospital on 26-Mar-2020.

On 29-Mar-2020, the patient was evaluated for uncontrolled abdominal cramping and pain. The patient reported the pain started the day prior, was localized to the whole abdomen, was non-radiating, and had no relieving factors. The pain was intermittent, severe, and rated at a 9/10 level. Acetaminophen was not providing any relief, but lorazepam improved her nausea. The patient also had loose stools and some diarrhea, with approximately seven stools over the past 24 hours. She denied fever or chills. The patient was placed on intravenous (IV) solumedrol and IV mycophenolate every eight hours. Tacrolimus was stopped on 31-Mar-2020 and sirolimus was started. On 01-Apr-2020, the patient underwent an esophagogastroduodenoscopy (EGD) which revealed Grade II GvHD of the gastrointestinal tract. The patient was started on a steroid wean on 04-Apr-2020 with the addition of budesonide and beclomethasone. She was discharged on 14-Apr-2020.

The patient was seen at a local hospital emergency room on 19-Apr-2020 for management of chest pain and shortness of breath. COVID-19 testing was performed and was negative. Bronchoscopy performed on 20-Apr-2020 revealed positivity for galactomannan. The fungal culture ended up growing *Penicillium.* Amphotericin B and micafungin were initiated as treatment. The patient was noted to have hemoptysis on 29-Apr-2020. A chest CT performed on the same day revealed an increase in the size and number of previously seen bilateral patchy pneumonic infiltrations with air bronchograms and air alveolograms. The patient underwent a bronchoalveolar lavage (BAL) which was consistent with diffuse alveolar hemorrhage. The BAL also revealed adenovirus. Peripheral blood was negative for adenovirus. The patient's respiratory status continued to decline which led to intubation. On 04-May-2020, the pulmonary team reported on a worsening chest x-ray which was thought to be due to the positive fluid balance despite less fresh blood than seen in the previous two days. The oxygen requirements were fluctuating between 50-60%. Additional bronchoscopy results were negative.

The patient had increasing oxygen requirements on 21-May-2020 despite no change in clinical status. Chest x-ray was stable when compared to the day prior. A CT scan of the chest completed on 22-May-2020 showed extensive interstitial infiltrates which appeared relatively dense in the right lower lung. The chest CT was repeated on 29-May-2020 and revealed marked worsening in the pulmonary infiltrates, a small pneumothorax, and impressive pneumomediastinum. Treatment with methylprednisolone 125 mg twice daily and ruxolitinib 5 mg twice daily was started on 03-Jun-2020. The patient became completely dependent on a non-rebreather mask. A CT scan of the chest on 05-Jun-2020 showed bilateral extensive interstitial infiltrates. The dose of steroids was increased for two days only since the impact of steroids could not be estimated at that time.

The medical team held a discussion at the bedside with the patient on 05-Jun-2020 regarding the goals of care. The team reviewed the progressive nature of the patient's idiopathic pulmonary syndrome and overall poor prognosis given her complete dependence on non-rebreather mask with 100% oxygen. At an additional meeting with the patient and her family on 10-Jun-2020 it was explained that any aggressive measures including intubation or cardiac resuscitation were unlikely to improve her condition. The patient agreed to change her code status to DNR/DNI. As the day progressed, the patient became more hypoxic and agreed to comfort measures only. She was taken to home hospice by ambulance and passed away later that night on 10-Jun-2020. Primary cause of death was noted as organ failure, pulmonary. An autopsy was not done.

Subject Identifier	GP3CMC-001
Age	21
Sex	Male
Baseline Weight (kg)	66.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	28 Jun 2019
Event	No SAEs Reported
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	

Date Of Death (If Applicable)
Narrative: Patient GP3CMC-001 is a 21 year-old White male with ALL who received an Unmanipulated CBU transplant on 28-Jun-2019. The patient was diagnosed with ALL on 20-Jun-2018. He underwent induction therapy with intrathecal cytarabine (20-Jun-2018), vincristine (20-Jun-2018, 03-Jul-2018, 10-Jul-2018, 16-Jul-2018), prednisone (20-Jun-2018 to 24-Jul-2018), daunorubicin (20-Jun-2018, 03-Jul-2018, 10-Jul-2018, 16-Jul-2018), peg-asparaginase (29-Jun-2018), and intrathecal methotrexate (03-Jul-2018, 24-Jul-2018). Consolidation therapy included dasatinib (27-Jul-2018 to 04-Oct-2018), cyclophosphamide (28-Jul-2018 to 05-Sep-2018), cytarabine (28-Jul-2018 to 31-Jul-2018, 06-Aug-2018 to 09-Aug-2018, 05-Sep-2018 to 09-Sep-2018, 12-Sep-2018 to 16-Sep-2018), mercaptopurine (27-Jul-2018 to 10-Aug-2018, 05-Sep-2018 to 12-Oct-2018), intrathecal methotrexate (30-Jul-2018, 06-Aug-2018, 13-Aug-2018, 18-Aug-2018), vincristine (11-Aug-2018, 18-Aug-2018, 19-Sep-2018, 26-Sep-2018), and pegasparagase (11-Aug-2018, 19-Sep-2018). Maintenance therapy included intrathecal methotrexate (12-Dec-2018), mercaptopurine (19-Oct-2018 to 21-Dec-2018), and methotrexate (19-Oct-2018 to 06-Jan-2019). Reinduction therapy included tisagenlecleucel (Kymriah) infusion on 15-Jan-2019 and 10-May-2019, with a preparative regimen consisting of cyclophosphamide and fludarabine. The patient had no reported past medical history. He had reported allergies to trimethoprim-sulfamethoxazole, corticosteroids, and chlorhexidine towelettes. Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (24-Jun-2019 to 27-Jun-2019), fludarabine (20-Jun-2019 to 22-Jun-2019), and cyclophosphamide (20-Jun-2019 to 21-Jun-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, acyclovir, voriconazole, and pentamidine. Neutrophil counts recovered at 28 days post-transplantation (26-Jul-2019). The patient was discharged from the hospital on 09-Aug-2019. There were no SAEs reported post-transplantation.

Subject Identifier	GP3CSA-001
Age	20
Sex	Male
Baseline Weight (kg)	52.3
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	07 Feb 2020
Event	Hyperacute GvHD
Severity	Grade 5
Serious (Yes/no)	Yes
Start/stop date of Event	03 Mar 2020 – 09 Mar 2020
Outcome Of Event	Death
Relationship To The Study Drug	Yes
Date Of Death (If Applicable)	09 Mar 2020
Narrative: Patient GP3CSA-001 is a 20 year-old White, Hispanic or Latino, male with ALL who received a Omidubicel transplant on 07-Feb-2020. The patient was diagnosed with Precursor B-Cell ALL on 29-Apr-2019. Pre-induction therapy was initiated on 29-Apr-2019. Day 1 of the BFM treatment plan started on 01-May-2019 and included prednisone, vincristine, daunorubicin, and L-asparaginase. The patient received intrathecal methotrexate on days 1, 8, 15, 22, and 29. A second cycle of induction with idarubicin, fludarabine, cytarabine, and G-CSF plus the addition of nilotinib was started on 11-Jun-2019. Maintenance therapy began on 16-Dec-2019 with mercaptopurine, vincristine, methotrexate, and prednisone. Salvage therapy was given with hyper-CVAD, nilotinib, and intrathecal chemotherapy through 11-Nov-2019 (start date unknown). The patient's past medical history included an infection requiring continuation of intravenous antimicrobial treatment (previous condition, absent	

at screening) and a venous thrombosis of the left lower limb. The patient had a reported allergy to platelet transfusions.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 40.25 mg/day (30-Jan-2020 to 01-Feb-2020), cyclophosphamide 3246 mg/day (30-Jan-2020 to 31-Jan-2020), and TBI 150 cGy (03-Feb-2020 to 06-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included posaconazole, acyclovir, trimethoprim/sulfamethoxazole, ciprofloxacin, and azithromycin. Neutrophil counts recovered at 20 days post-transplantation (27-Feb-2020).

In the days following transplant, the patient experienced febrile neutropenia with negative cultures, and facial edema in the submandibular region. All symptoms improved after treatment with broad-spectrum antibiotic therapy despite the absence of a clear etiological source. Over the course of the next two weeks, the patient began to experience an increase in nausea, vomiting, and diarrhea. Stool output was >1300 mL per day with vomiting >1500 mL per day. The patient also had an increase in weight greater than 10% and reported hepatic pain. Pain was addressed with intravenous analgesics. An ultrasound of the abdomen on 19-Feb-2020 showed hepatosplenomegaly and there was a concern of veno-occlusive disease/sinusoidal occlusive syndrome. Treatment with defibrotide was initiated on 21-Feb-2020.

The patient was noted to be febrile on 23-Feb-2020 (post-transplant day +16). Cultures were drawn and empiric antibiotics were continued, with the addition of colistin and the discontinuation of cyclosporine due to worsening kidney function. The following day, the patient was noted to have a disseminated morbilliform rash, with palmar and plantar hyperemia compromising about 85% of the body surface area. The rash was reported as consistent with hyperacute GvHD (stage III of skin and grade IIb overall). GvHD of the skin was confirmed by punch biopsy on 24-Feb-2020. Methylprednisolone and sirolimus were started on 25-Feb-2020. The patient continued to have persistent cutaneous involvement, worsening transaminases, and hyperbilirubinemia. This was suggestive of hepatic involvement of GvHD refractory to corticosteroid therapy.

Treatment for refractory hyperacute GvHD Grade IV of the skin, gastrointestinal tract, and liver was initiated on 29-Feb-2020 with etanercept and continued sirolimus. The goal was to intensify immunosuppression in anticipation of treatment with extracorporeal photopheresis (ECP). On 01-Mar-2020, the patient tested positive for *Clostridium difficile* which was treated with metronidazole. Due to the lack of response, a worsening clinical picture, and thrombocytopenia, the defibrotide was stopped after 11 doses on 02-Mar-2020. Ursodiol dose was increased.

On 03-Mar-2020, the patient developed hypoxemic respiratory failure followed by hemodynamic instability. He required endotracheal intubation and hemodynamic support with the use of vasopressors in the ICU. Given the hemodynamic instability and poor prognosis, plans for therapy with ECP were cancelled. The patient remained in the ICU with progressive multiple organ failure and severe acute GvHD (Grade IV). The patient died on 09-Mar-2020. Primary cause of death was noted as acute GvHD. An autopsy was not done.

Subject Identifier	GP3CSP-001
Age	14
Sex	Female
Baseline Weight (kg)	70.6
Race	Black – South or Central American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	19 Dec 2019
Event	1. Encephalitis 2. Catheter-Related Infection
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes

	2. Yes
Start/stop date of Event	1. 10 Feb 2020 – 03 Mar 2020 2. 15 Jun 2020 – 24 Jun 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	
Narrative: Patient GP3CSP-001 is a 14 year-old Black, South or Central American, female with Dendritic Cell Leukemia who received a Omidubicel transplant on 19-Dec-2019. The patient was diagnosed with Dendritic Cell Leukemia, with extramedullary skin involvement, on 21-Feb-2019. She underwent treatment according to protocol BFM 2009 HR. Reinduction with idarubicin, fludarabine, cytarabine, and G-CSF was also given. The patient's medical history included severe pulmonary impairment (DLCO 54%) at study screening. Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 47 mg/day (12-Dec-2019 to 14-Dec-2019), cyclophosphamide 4500 mg/day (12-Dec-2019 to 13-Dec-2019), and TBI 200 cGy (16-Dec-2019 to 18-Dec-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, trimethoprim/sulfamethoxazole, amoxicillin, voriconazole, and ciprofloxacin. Neutrophil counts recovered at seven days post-transplantation (26-Dec-2019). The patient was discharged from the hospital on 21-Jan-2020. The patient was admitted on 10-Feb-2020 due a fever of unknown origin. She was noted to have non-microbiologically defined encephalitis. The patient was treated with foscarnet, meropenem, and cefepime. She was discharged from the hospital on 13-Mar-2020. The patient was admitted on 15-Jun-2020 due to an infection noted at the insertion site of her central line catheter. She was treated with cefepime and teicoplanin for ten days. The catheter-related infection was considered resolved on 24-Jun-2020.	

Subject Identifier	GP3DCH-001
Age	20
Sex	Male
Baseline Weight (kg)	112.0
Race	White - South or Central American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	01 Nov 2019
Event	1. Skin GvHD 2. Viral Infection
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 21 Nov 2019 – 26 Nov 2019 2. 07 Jan 2020 – 13 Jan 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	
Narrative:	

Patient GP3DCH-001 is a 20-year-old White, South or Central American, Hispanic or Latino male with ALL who received a Omidubicel transplant on 01-Nov-2019.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor B-Cell ALL) on 30-Jul-2018. He underwent one cycle of induction therapy per COG roadmap AALL1131 (01-Aug-2018 to 29-Aug-2018), two cycles of consolidation therapy per COG AALL1131 (cycle 1: 04-Sep-2018 to 24-Sep-2018; cycle 2: 01-Oct-2018 to 29-Oct-2018), and three cycles of maintenance therapy per COG roadmap AALL1131 (cycle 1: 29-Oct-2018 to 04-Dec-2018; cycle 2: 14-Dec-2018 to 29-Dec-2018; cycle 3: 03-Jan-2019 to 11-Feb-2019). On 19-Mar-2019 the patient received an autologous CAR-T infusion with cyclophosphamide/fludarabine preparative regimen. B cells returned four months post initial infusion. The patient then underwent a second autologous CAR-T infusion with cyclophosphamide/fludarabine preparative regimen on 15-Jul-2019. The patient's past medical history included transaminitis and obesity (BMI = 38.4 kg/m^2). He had moderate hepatic and moderate pulmonary impairment at study screening. The patient had reported allergies to corticosteroids, ondansetron, and packed blood red cells (hives with administration).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 200 cGy/day (28-Oct-2019 to 30-Oct-2019), fludarabine 58 mg/day (24-Oct-2019 to 26-Oct-2019), and cyclophosphamide 4716 mg/day (24-Oct-2019 to 25-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included micafungin, trimethoprim-sulfamethoxazole, and acyclovir. Neutrophil counts recovered at nine days post-transplantation (10-Nov-2019). The patient was discharged from the hospital on 19-Nov-2019.

On 21-Nov-2019, the patient was found to be febrile with a new rash covering more than 50% of his body surface area at a scheduled follow-up outpatient clinic visit. The patient was given a dose of cefepime after blood cultures were obtained. He was admitted inpatient on 21-Nov-2019 for management and evaluation of suspected acute skin GvHD. On the date of admission, a punch skin biopsy was performed using a sample obtained from the right forearm. Results showed interface dermatitis consistent with Grade II GvHD. The patient was treated with intravenous methylprednisolone, and topical hydrocortisone 1% and triamcinolone 0.1% creams three times a day, with improvement and the beginning of resolution of the rash.

The patient was monitored for reactivation of HHV6, CMV, EBV and adenovirus while on steroids, all which remained inactive. On 26-Nov-2019, the patient's intravenous methylprednisolone doses were converted to oral doses with taper and he was discharged home. The rash at discharge was noted to be erythematous with peeling on both hands but mostly resolved per assessment of the treating team.

On 07-Jan-2020 the patient presented to the outpatient clinic with new onset of fever associated with worsening cough and upper respiratory infection symptoms. He was admitted, blood cultures and nasal wash were obtained, and cefepime was started. Nasal wash was found to be positive for Influenza B, Adenovirus, and Rhinovirus. On 07-Jan-2020 blood cultures from the central line were positive for *Staph epidermidis*. On 08-Jan-2020 only one of two cultures were positive, and on 09-Jan-2020 and 10-Jan-2020 all cultures were negative. The patient had his last fever on 10-Jan-2020.

The patient was treated with empiric cefepime and vancomycin from 07-Jan-2020 to 10-Jan-2020. When sensitivities to *Staph epidermidis* returned on 10-Jan-2020 the patient was transitioned to levofloxacin for 14 days. The patient was continued on his prophylactic acyclovir and letermovir. Voriconazole was switched to micafungin prophylaxis given the patient's previous history of transaminitis. The patient was discharged on 13-Jan-2020.

Subject Identifier	GP3DCH-002
Age	17
Sex	Female
Baseline Weight (kg)	103.0
Race	White
Study Therapy	Omidubicel

Date Of Study Therapy Administration	18 Dec 2019
Event	1. Hypertension 2. AKI 3. Cord Colitis 4. Norovirus Infection
Severity	1. Grade 3 2. Grade 3 3. Grade 2 4. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 17 Jan 2020 – 22 Jan 2020 2. 07 Feb 2020 – 08 Feb 2020 3. 18 Feb 2020 – 13 May 2020 4. 02 Dec 2019 – 03 Dec 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved
Relationship To The Study Drug	1. No 2. No 3. Yes 4. NA: Pre-transplant event
Date Of Death (If Applicable)	

Narrative:
Patient GP3DCH-002 is a 17 year-old White female with AML who received a Omidubicel transplant on 18-Dec-2019.

The patient was diagnosed with AML [AML with 11q23 (MLL) abnormalities] on 28-Aug-2019. She underwent induction therapy with protocol AAML0531 including intravenous (IV) cytarabine, daunorubicin, gemtuzumab, and intrathecal cytarabine (31-Aug-2019 to 27-Sep-2019). Induction II therapy included IV cytarabine, daunorubicin, and intrathecal cytarabine (10-Oct-2019 to 18-Oct-2019). The patient's past medical history included perineum cellulitis (05-Sep-2019) and pancreatitis (15-Sep-2019). She was hospitalized for norovirus gastroenteritis from 02-Dec-2019 to 03-Dec-2019. Surgical history included tonsillectomy and adenoidectomy (Nov-2008). The patient had reported allergies to gemtuzumab ozogamicin.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 99 mg/day (13-Dec-2019 to 15-Dec-2019), thiotepa 405 mg/day (11-Dec-2019 to 12-Dec-2019), and busulfan 259 - 405 mg/day (13-Dec-2019 to 15-Dec-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included trimethoprim-sulfamethoxazole, micafungin, and acyclovir. Neutrophil counts recovered at 13 days post-transplantation (31-Dec-2019). The patient was discharged from the hospital on 07-Jan-2020.

On 17-Jan-2020 the patient developed nausea, abdominal pain, facial tingling, and hypertension up to the 170s/110s during pentamidine infusion. Initially the hypertension was felt to be related to anxiety and pain related to the pentamidine reaction, however it persisted despite diphenhydramine, lorazepam, and significant calming down of the patient. The hypertension was treated with hydralazine and the patient was admitted to the inpatient floor. The patient required 1-2 doses of nifedipine daily until 20-Jan-2020. Amlodipine was restarted on 20-Jan-2020 with 5 mg at bedtime and there was subsequent improvement in blood pressures. The patient was discharged on 22-Jan-2020 with plans to continue daily amlodipine.

The patient was then found to have an elevated creatinine of 2.33 mg/dL on 07-Feb-2020 during a routine post-BMT clinic appointment. The patient received an IV bolus of fluids and the lab test was repeated four hours

later which showed a level of 2.48 mg/dL. Another sample sent 7.5 hours later showed a creatinine of 1.99 mg/dL. The patient complained of severe abdominal pain. She was admitted for monitoring and fluid support. After 24 hours of monitoring, the serum creatinine continued to decline – 1.59 mg/dL, and then 1.12 mg/dL. The patient did not require any interventions outside of hospitalization for supportive care and was discharged on 08-Feb-2020 at which point the AKI was noted to be resolved.

On 18-Feb-2020, the patient presented to the clinic with diarrhea, vomiting, abdominal cramps, headache, nasal congestion, rhinorrhea, pharyngitis, and oral intake intolerance. She was afebrile. The patient was admitted on 18-Feb-2020 for medical monitoring and fluid administration. Stool output was approximately 1200 mL over the next 24 hours. Electrolytes remained stable. Infectious workup included a RVP, strep swab, and gastrointestinal (GI) panel all of which were negative. The patient continued her home dose of cyclosporine and had a therapeutic level of 205 ng/mL on 20-Feb-2020. Given the potential benefit of therapy outweighing the risks of an antibiotics course, the patient was started on treatment for cord colitis on 20-Feb-2020 with levofloxacin and metronidazole.

On 21-Feb-2020, the patient underwent an upper GI endoscopy and colonoscopy that were negative for infection and GvHD. The intra-operative findings were non-specific but did show mild colitis as well as upper GI tract erythema without ulcerations. Abdominal pain was managed with a regimen of acetaminophen and hydromorphone as needed. The patient's diarrhea improved, and she was stable for discharge home on 22-Feb-2020. The patient finished the 14-day antibiotic course of levofloxacin and metronidazole on 04-Mar-2020.

The patient continued to have intermittent abdominal pain and diarrhea after discharge. She was evaluated on 08-Apr-2020 (telehealth visit) and reported episodic abdominal pain that occurred approximately once a week. The events were self-resolving and required no interventions. The patient was started on a cyclosporine taper of 150 mg BID (22-Feb-2020 to 11-Mar-2020), 125 mg/day for 1 week (11-Mar-2020 to 18-Mar-2020), 100 mg/day for three weeks (18-Mar-2020 to 08-Apr-2020), and 75 mg/day (08-Apr-2020). The patient was seen by the BMT staff via telehealth video visit on 15-May-2020. There were no new concerns for symptoms of GvHD or infection. The cyclosporine taper ended on 13-May-2020. The cord colitis event was reported as resolved as of 13-May-2020.

Subject identifier	GP3DFC-001
Age	48
Sex	Male
Baseline weight (kg)	83.7
Race	White
Study therapy	Omidubicel
Date of study therapy administration	26 Jan 2018
Event	1. Fever 2. Acute Onset CKD 3. Respiratory Failure
Severity	1. Grade 1 2. Grade 3 3. Grade 4
Serious (yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 11 Feb 2018 – 15 Feb 2018 2. 24 Oct 2018 – 26 Oct 2018 3. 24 Dec 2018 – 05 Jan 2019
Outcome of event	1. Resolved 2. Resolved with sequelae 3. Resolved with sequelae
Relationship to the study drug	1. No 2. No

	3. No
Date of death (if applicable)	04 Dec 2020

Narrative:
Participant GP3DFC-001 is a 48 year-old white male with Acute Lymphoblastic Leukemia who received an omidubicel transplant on 26-Jan-2018.

The participant was diagnosed with Acute Lymphoblastic Leukemia (Precursor T-cell ALL) on 27-Aug-2007. He developed findings suggestive of tumor lysis syndrome which required hemodialysis. He was treated with hyper-CVAD for four cycles (Apr-2008) which led to complete remission and maintenance therapy with 6-mercaptopurine/methotrexate for two years (2008). He then developed a right tonsillar mass and biopsy was consistent with recurrent ALL in Aug 2017. The participant then received therapy with ECOG 1910 for three cycles (12-Sep-2017). The participant's past medical history included moderate pulmonary impairment (CDLCO 79%) and factor V Leiden associated deep vein thrombosis. Surgical history included tonsillectomy.

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of total body irradiation 165 cGy/day (22-Jan-2018 to 25-Jan-2018), fludarabine 51 mg/day (19-Jan-2018 to 21-Jan-2018), and cyclophosphamide 5200 mg/day (19-Jan-2018 to 20-Jan-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Other medications included clobetasol, compazine, folic acid, magnesium oxide, multivitamin, stannous fluoride, furosemide, atovaquone, fluconazole, acyclovir, and labetalol. Neutrophil counts recovered at nine days post-transplantation (03-Feb-2018). The participant was discharged from the hospital on 06-Feb-2018.

Post-transplantation the participant was hospitalized for pyrexia (11-Feb-2018 to 15-Feb-2018) and acute kidney injury (24-Oct-2018 to 26-Oct-2018) for which tacrolimus was stopped. The participant was then admitted on 24-Dec-2018 for management of acute hypoxemic respiratory failure. The participant presented with a two-day history of progressively worsening shortness of breath and cough with purulent sputum production. In the emergency department, he was stable but tachypneic to 45. His bicarbonate was low at 8 and his WBC were 14,000. Chest x-ray showed diffuse bilateral alveolar opacities. The participant was placed on BiPAP and given IV furosemide. He was admitted for management of acute hypoxemic respiratory failure and started on hemodialysis for acidosis and volume management.

The participant was found to have a positive urine strep antigen and suspected *Pneumocystis* pneumonia (PCP). He was treated for PCP with trimethoprim-sulfamethoxazole and steroids though no PCP was found. He was found to have a right upper lobe pulmonary embolism on chest CT angiography on 29-Dec-2018. The participant was discharged on 05-Jan-2019 to continue dialysis as an outpatient. At discharge, he had some hypoxia on exertion without symptoms (initially 79% on room air, repeat spirometry was 86% on room air). Saturations at rest were 94-95%. The respiratory failure event was considered resolved on 05-Jan-2019.

The participant died on 04-Dec-2020 due to a viral infection.

Subject Identifier	GP3DFC-002
Age	33
Sex	Male
Baseline Weight (kg)	67.7
Race	Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	02 Mar 2018
Event	No events
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	

Narrative:
Patient GP3DFC-002 is a 33 year-old Asian male with ALL who received an Unmanipulated CBU transplant on 02-Mar-2018.

The patient was diagnosed with ALL on 21-Aug-2013. He underwent induction therapy with daunorubicin, cytarabine, prednisone, and intrathecal methotrexate (Aug-2013). He underwent consolidation therapy with intrathecal methotrexate, cyclophosphamide, cytarabine, 6-mercaptopurine, vincristine IV, and PEG-asparaginase (07-Oct-2013). Maintenance therapy included intrathecal methotrexate, vincristine IV and methotrexate, and PEG-asparaginase (23-Dec-2013) and 6-MP, decadron, methotrexate by mouth, and vincristine and intrathecal methotrexate (07-Jul-2014). Reinduction therapy included vincristine, dexamethasone, intrathecal cytarabine, and blinatumomab (28-Sep-2017) and three cycles of inotuzumab (Nov-2017). The patient's past medical history included multiple cerebral infarcts (19-Mar-2014) with associated coma for 10 days and mechanical ventilation. He had moderate pulmonary impairment at study screening. The patient's surgical history included bilateral hip arthroplasty and right total shoulder replacement. The patient had reported allergies to adhesive/latex/natural rubber, diphenhydramine, cefepime, fosaprepitant, and pegaspargase.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (26-Feb-2018 to 01-Mar-2018), fludarabine (23-Feb-2018 to 25-Feb-2018), and cyclophosphamide (23-Feb-2018 to 24-Feb-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, trimethoprim-sulfamethoxazole, micafungin, and levofloxacin. Neutrophil counts recovered at 35 days post-transplantation (06-Apr-2018). The patient was discharged from the hospital on 12-Apr-2018. The patient had no reported SAEs post-transplantation.

Subject Identifier	GP3DFC-003
Age	23
Sex	Male
Baseline Weight (kg)	58.2
Race	Middle Eastern
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	30-Mar-2018
Event	1. Intractable nausea 2. Idiopathic pneumonia non-infectious
Severity	1. Grade 3 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 08 May 2018 – 19 May 2018 2. 26 Jun 2018 – 17 Aug 2018
Outcome Of Event	1. Resolved 2. Death
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	17-Aug-2018

Narrative:
Patient GP3DFC-003 is a 23 year-old Middle Eastern male with B-Cell ALL who received a Unmanipulated CBU transplant on 30-Mar-2018.

The patient was diagnosed with B-Cell ALL on 23-Jul-2017. He was treated with first line chemotherapy in Aug-2017. He received methotrexate, cytarabine, and methylprednisone. It is unclear whether treatment included dasatinib. He received a total of ten intrathecal chemotherapies secondary to CNS involvement (meningeal enhancement), with complete remission noted by 31-Aug-2017. On 09-Jan-2018, the patient was diagnosed with ALL relapse. Second line chemotherapy with HiDAC for marrow/extramedullary disease was given in Jan-2018, with intrathecal treatment with methotrexate (3 doses) and cytarabine (1 dose) given for

CNS relapse (between Jan and Mar-2018). Second remission with incomplete marrow recovery (CRi) was noted on 03-Mar-2018. The patient's medical history included anxiety, asthma, seizures, necrotizing pancreatitis, and diminished pulmonary function - FEV1 92% and cDLCO 41% of predicted. A review of his medical records revealed an additional history of low back pain with sclerotic changes which preexisted his ALL involvement of the 5th lumbar vertebra.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of eight 165 cGy doses of TBI (26-Mar-2018 to 29-Mar-2018), fludarabine 43 mg/day (23-Mar-2018 to 25-Mar-2018), and cyclophosphamide 3700 mg/day (23-Mar-2018 to 24-Mar-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included trimethoprim-sulfamethoxazole, acyclovir, micafungin, levofloxacin, and fluconazole. Neutrophil counts recovered at 20 days post-transplantation (19-Apr-2018). The patient was discharged from the hospital on 24-Apr-2018.

The patient's post-transplant course was remarkable for two episodes of infection (Grade 1 hepatic infection on 20-Mar-2018 with organism not specified and Grade 1 staphylococcus coag + blood infection on 04-Apr-2018). The patient had an admission on 05-May-2018 for intractable nausea and failure to thrive, which was resolved at the time of discharge on 19-May-2018. During the admission, the patient had an endoscopy and GvHD was ruled out. At that time mycophenolate mofetil was discontinued and tacrolimus dosing was decreased due to elevated creatinine.

The patient was then admitted on 26-Jun-2018 for management of septic shock. The patient was seen in the study clinic on 26-Jun-2018 and reported new onset headache for 7-10 days and a 3-day history of feeling unwell, poor oral intake, subjective chills, and associated progressive shortness of breath, productive cough, and pleuritic chest pain. He also described recent secondhand exposure to smoke and possible asthma exacerbation. The patient was referred for same day evaluation at the local ED. Vitals at the time were temperature 37.1◦C, heart rate ~140 bpm, blood pressure 82/49 mmHg, respiratory rate 20 breaths per minute, and oxygen saturation (SpO2) on room air of 83%. Nasal cannula oxygen supplementation at 3 liters resulted in saturation improvement to only 93%. The patient received nebulizer treatments, IV methylprednisolone, and magnesium oxide for treatment of a possible asthma exacerbation. However, chest CT revealed multifocal infiltrates and bilateral pleural effusions. He was subsequently admitted to the hospital on 26-Jun-2018 for suspicion of bacterial pneumonia superimposed on an asthma exacerbation.

The patient was initiated on antibiotic coverage for community-acquired and nosocomial pathogens with cefepime, vancomycin, and azithromycin. Viral prophylaxis with acyclovir and letermovir was continued, with the addition of bacterial prophylaxis using trimethoprim/sulfamethoxazole. Workup on 29-Jun-2018 demonstrated the patient to be negative for beta-D-glucan and galactomannan, adenovirus antibody, CMV DNA, legionella antigen, parainfluenza 1-3 antibodies and antigens, RSV antigen, influenza A and B antigens, and streptococcal pneumonia antigen. On 30-Jun-2018, the patient exhibited worsening hypoxemia and increased work of breathing, despite a lack of significant radiographic progression on chest x-ray and no evidence of pneumothorax. Cultures remained negative. Glucan and galactomannan were negative. Accordingly, concern for involvement with a non-infectious post-BMT process such as IPS, less likely DAH was raised. The patient was subsequently intubated, controlled ventilation initiated, and bronchioalveolar lavage performed. Antibiotic coverage with cefepime, vancomycin, and azithromycin was continued, supplemented with airway bronchodilators and prednisone 40 mg BID. On 01-Jul-2018, the patient exhibited overall improvement in his supplemental oxygen requirement and chest x-ray. Ventilatory mechanics demonstrated decreased compliance but no evidence of increased airway resistance, so pressure support ventilation was initiated. Cultures remained negative, including glucan and galactomannan, and bronchoscopy results were not consistent with DAH. On 01-Jul-2018, the patient self-extubated and was noted on 02-Jul-2018 to be saturating at 99-100% on 4 liters nasal cannula oxygen. Lung examination was improved with no evidence of pulmonary embolism on CT imaging.

The patient was transferred back to the BMT unit on 02-Jul-2018 and was stable on room air. Infectious workup was negative. He complained of diffuse muscle pain and his WBC was dropping without a clear source. On 10-Jul-2018, he developed an increased FiO2 requirement and increased work of breathing. Antibiotics were broadened to vancomycin and azithromycin. He was started on solumedrol and lasix. Chest CT showed progressive bilateral opacities. He was transferred back to the MICU and intubated for worsening hypoxemic

respiratory failure. There was significant improvement in oxygenation with P/F 360, and significant radiographic improvement. On 12-Jul-2018, he tolerated a spontaneous breathing test. However, he became more uncomfortable and agitated, requiring increased fentanyl and propofol. He was placed back on Assist-Control Ventilation. He was extubated on 13-Jul-2018 and transferred back to the BMT ward. He had multiple episodes of severe acute hypoxemia and had diffuse ground-glass opacities on imaging. Bronchoscopy was unrevealing. transthoracic echocardiogram (TTE) with bubble performed showed no evidence of shunt. CT showed evidence of a chronic pulmonary embolism (PE) but no acute finding. He had elevated aldolase and low creatinine phosphokinase (CPK). Pulmonary consult was obtained on 19-Jul-2018.

On 22-Jul-2018, the patient was tripoding, tachycardic, desaturating, and using accessory muscles to breathe. He was intubated, sedated, and transferred back to MICU. The patient had multiple MICU admissions for respiratory failure. A chest CT on 01-Aug-2018 showed mildly increased ground-glass opacities. His beta-d-glucan was elevated to 93. His immunosuppression included methylprednisone 2 mg/kg qd, status post 2x tocilizumab and etanercept. Repeat infectious workup was notable for gram positive cocci (NOS). Transthoracic echo showed small to moderate pericardial effusion with no evidence of tamponade. On 06-Aug-2018, suspicion for infection was low and the high volume of antibiotics was mildly interfering with attempted diuresis so the patient was de-escalated off cefepime and treatment dose trimethoprim-sulfamethoxazole. On 07-Aug-2018, the patient's blood glucan was down trending. Flu, HMPV, and RSV were negative. Per ID consult, all antibiotics were discontinued. The patient underwent aggressive diuresis of about 2 L over two days with little improvement in O2 requirements. He was given one dose of tocilizumab. His ABG showed hypoxemic, hypercarbic metabolic acidosis.

At a goals of care meeting, the patient wanted to be intubated. He was intubated on 10-Aug-2018 with AC-VC mode. He was difficult to ventilate secondary to high peak inspiratory pressure (PIP) with poor lung compliance. He was sedated initially with propofol, but he developed hypertriglyceridemia, and the sedation was changed to midazolam. The patient was also continued on a fentanyl drip. The patient's family requested to transfer him back to a local area hospital and declined terminal extubation. However, they wanted him transitioned to DNR/DNI status. In the days following intubation, he became increasingly hyperkalemic and acidemic and was requiring increasing doses of pressors to maintain goal mean arterial pressures. By 17-Aug-2018, he was on vasopressin, norepinephrine, and epinephrine at maximal doses and receiving calcium gluconate, insulin, dextrose, and kayexalate. He then became hypotensive, refractory to maximum dose of pressors, and became increasingly bradycardic until he passed away on 17-Aug-2018. Primary cause of death was noted as IPS (not infectious in origin). Autopsy was declined by the family.

Deviations with potential medical significance: The patient had a cDLCO of 41% at the time of randomization. This protocol exemption was approved by both the site IRB and the sponsor prior to randomization. Mycophenolate mofetil was not given per protocol during days 0-21. Mycophenolate mofetil was dosed "per institutional standard" (1000 mg IV q8H) and was not changed due to a toxicity. The patient's calculated dose per the protocol was 930 mg (<10% difference).

Subject Identifier	GP3DFC-004
Age	45
Sex	Female
Baseline Weight (kg)	54.5
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	29 Jun 2018
Event	Hemorrhagic Cystitis
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	29 Aug 2018 – 04 Sep 2018
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3DFC-004 is a 45 year-old White, Hispanic or Latino female with ALL who received an Unmanipulated CBU transplant on 29-Jun-2018

The patient was diagnosed with ALL on 09-Mar-2016. She underwent induction therapy with six cycles of CALGB (Mar-2016), maintenance therapy with 6-Mercaptopurine vincristine methotrexate prednisone (POMP) (Feb-2017), and reinduction therapy with hyper-CVAD-B cycle (22-Jan-2018 and 01-Mar-2018). The patient's past medical history included moderate pulmonary impairment at screening (DLCO 73% of predicted). Surgical history included Essure tubal ligation (2012), back surgery for lumbar spine herniated disk (2008), and lumbar discectomy of L5S1 (2008).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (25-Jun-2018 to 28-Jun-2018), fludarabine (22-Jun-2018 to 24-Jun-2018), and cyclophosphamide (22-Jun-2018 to 23-Jun-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, trimethoprim-sulfamethoxazole, and levofloxacin. Neutrophil counts recovered at 14 days post-transplantation (13-Jul-2018). The patient was discharged from the hospital on 13-Aug-2018.

The patient was admitted on 29-Aug-2018 for recurrent and worsening hemorrhagic cystitis with low BP, 5-point hematocrit drop, and dizziness. The hemorrhagic cystitis was secondary to BK virus. Symptoms were controlled with platelet and PRBC transfusions. On 01-Sep-2018 the patient reported an improvement in clots. On 02-Sep-2018 she received a large volume of IV fluid. The BK virus was found to be down trending. On 04-Sep-2018 the patient's symptoms improved, and PO intake was sufficient for discharge.

Subject identifier	GP3DFC-006
Age	52
Sex	Male
Baseline weight (kg)	76.6
Race	White
Study therapy	Omidubicel
Date of study therapy administration	14 Sep 2018
Event	Pneumonitis
Severity	Grade 5
Serious (yes/no)	Yes
Start/stop date of Event	31 Dec 2018 – 29 Jun 2019
Outcome of event	Death
Relationship to the study drug	No
Date of death (if applicable)	29 Jun 2019

Narrative:
Patient GP3DFC-006 is a 52 year-old White male with ALL who received a Omidubicel transplant on 14-Sep-2018.

The patient was diagnosed with ALL on 27-Feb-2018. He was started on Larsen CALGB9111 on 01-Mar-2018 and imatinib on 13-Mar-2018 when t9:22 returned positive. He received a dose of intrathecal methotrexate on 21-Mar-2018. Bone marrow biopsy on 06-Apr-2018 showed partial remission and persistent Ph+ ALL. The patient underwent consolidation therapy in May-2018 with hyper-CVAD (cyclophosphamide, vincristine, adriamycin, and dexamethasone) and two courses of ponatinib. Starting on 24-Jul-2018 he underwent one cycle of blinatumomab with BM biopsy showing morphological remission. The patient's past medical history included aortic aneurysm (<5.0 cm), bicuspid aortic valve, gastroesophageal reflux disease, childhood asthma, and depression. At screening he had moderate pulmonary impairment. Surgical history included esophageal dilation in 2010.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (10-Sep-2018 to 13-Sep-2018), fludarabine 53 mg/day (07-Sep-2018 to 09-Sep-2018),

and cyclophosphamide 5480 mg/day (07-Sep-2018 to 08-Sep-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 35 days post-transplantation (19-Oct-2018). The patient was discharged from the hospital on 17-Oct-2018.

The patient was admitted on 31-Dec-2018 for management of a lower respiratory tract infection. The patient presented with fever and right-sided chest pain. He was found to be neutropenic with an ANC of 500. The patient reported feeling febrile on and off for several weeks and had a temperature between 99 to 100°F. He reported associated congestion and non-productive cough which was more prevalent at night. He had no history of hemoptysis. He reported right-sided "lung pain" pleuritic in nature and dyspnea on exertion. In the ED, the patient had a negative flu swab, urinalysis, and unremarkable chest x-ray. Blood and urine cultures were taken. He was started on intravenous (IV) vancomycin, cefepime, and a one liter lactated ringer bolus. The patient's IV trimethoprim-sulfamethoxazole (Bactrim) was then switched to oral Bactrim.

Blood and urine cultures showed no growth at 48 hours. The patient was treated with vancomycin and cefepime for seven days and was given filgrastim. His symptoms resolved, and on 07-Jan-2019 he was switched to levofloxacin to finish a 14-day course of antibiotics. He continued to have minimal shortness of breath and cough, but his symptoms continued to improve. His WBC count increased to an ANC of 1400 on the day of discharge. The patient had AKI during his hospital stay with a peak creatinine of 1.6 mg/dL. His creatinine was back down to 1.2 mg/dL on the day of discharge. He was in good condition on the day of discharge (07-Jan-2019).

On 08-Feb-2019, the patient was readmitted to the hospital for suspicion of catheter-related infection. Blood cultures from 05-Feb-2019 had been found to be positive for gram-negative rods. The bacteremia was thought to be most likely from a pulmonary source as the patient had a persistent dry cough since January and lacked other signs or symptoms of an alternative source. On admission peripheral and central blood cultures were repeated and were negative at 48 hours. On presentation, the patient was pancytopenic with a WBC count of 1000. He was started on cefepime then transitioned to azithromycin and piperacillin-tazobactam (Zosyn) for concern of possible aspiration pneumonia. The patient developed neutropenia during his hospital stay and was given filgrastim. The patient improved and his ANC on discharge was trending up to 1.36. He was discharged on 11-Feb-2019 to complete a 10-day course of ciprofloxacin.

The patient was then readmitted on 14-Feb-2019. He had locally worsening infiltrates and fevers. A diagnosis of pneumonitis was made on 15-Feb-2019. The patient was intubated on 15-Feb-2019 for respiratory failure. He had a tracheostomy done on 03-Mar-2019. Bronchoalveolar lavage done on 04-Mar-2019 was positive for gram-negative rods (*Klebsiella*). A CT chest done on 07-Mar-2019 showed diffuse ground-glass changes, septal thickening, traction bronchiectasis, and possible early honeycombing with persistent interstitial pattern consistent with pulmonary GvHD. The patient received two bursts of pulse dose steroids with tocilizumab. A prednisone taper was initiated on 10-Mar-2019. The patient was then discharged from his local hospital on 16-Mar-2019 and transferred to the original transplant center.

The patient was transferred to the original transplant center on 17-Mar-2019. A repeat CT chest done on 17-Mar-2019 showed mild improvement of the diffuse ground-glass attenuation, consolidation most consistent with pneumonia, and possible superimposed mild edema or diffuse alveolar damage. The patient's respiratory course was complicated by agitation that required frequent increases in propofol. A brain MRI was done and showed subacute left cerebellar infarct. The findings did not explain the patient's altered mental status and was considered most likely incidental. Blood cultures were positive for gram positive cocci in pairs and clusters. The patient was started on vancomycin. Serial cultures showed growing 3+ *Klebsiella*. He was considered a likely colonizer and antibiotics were discontinued. His tacrolimus was stopped on 18-Mar-2019. The patient was started on posaconazole for fungal prophylaxis. A CBC done on 18-Mar-2019 showed pancytopenia and the patient was started on tbo-filgrastim (Granix) on 20-Mar-2019.

CT chest done on 21-Mar-2019 showed worsening bilateral consolidations with lower lobe predominance reflective of multifocal pneumonia consistent with known *Klebsiella* pneumonia (diffuse ground-glass opacity). PEG placement was done on 28-Mar-2019 for tube feeding. The patient's respiratory status improved as of 01-Apr-2019. Granix was stopped on 01-Apr-2019. The patient continued to have improvements in

respiratory status and strength, tolerating pressure support for longer periods of time. A repeat CT chest showed improved consolidations, but there was remaining diffuse ground-glass opacities and some pulmonary edema. As of 07-Apr-2019, the patient was stable on ventilatory support and was awaiting placement at a long-term rehab facility.

On 20-Apr-2019, the patient developed worsening pulmonary status. He had a bronchoscopy with no mucous plugging or evidence of PE. His lungs showed pulmonary edema and worsening lung mechanics. Given a concern that volume was likely a contributing factor, the patient was restarted on active IV diuresis with furosemide (Lasix). Sputum bronchoalveolar lavage culture on 24-Apr-2019 was positive for *Klebsiella* that was cefepime and meropenem susceptible. The patient was treated with vancomycin and cefepime for ventilator-associated pneumonia (VAP). Vancomycin was stopped when blood cultures showed no growth.

As of 01-May-2019, the patient's respiratory status improved to baseline with mucus suctioning. However, suctioning needs were still too high for transfer to rehab facility. On 09-May-2019, suctioning needs were acceptable for the patient to be discharged to long-term rehab facility.

The patient was then readmitted to the original transplant center on 20-Jun-2019 for VAP. His respiratory status had acutely declined over 4 days prior to admission. The patient was found to be in hypoxic respiratory failure when he arrived in the ED. He was initially placed on AC/VC which the patient did not tolerate. He was then placed on AC/PC with initial settings of 24/7 with oxygen saturations at 92% and tidal volume around 300 ml. Blood cultures were drawn, and the patient was started on cefepime and vancomycin for concern of *Klebsiella* sepsis given his recent history. On 24-Jun-2019, the patient went into atrial fibrillation with rapid ventricular response, acutely decompensating and requiring pressors. He had decreased urine output on 25-Jun-2019 after receiving large volumes of fluids on 24-Jun-2019.

Starting 26-Jun-2019, the patient progressively developed worsening hypoxemia and increasing pressor requirements. He developed flash pulmonary edema on 27-Jun-2019 and was started emergently on CVVH. Over the next two days he developed worsening acidemia, requiring CVVH, calcium chloride, bicarbonate, and maxed out pressors. The patient was then converted to DNR/DNI. The patient passed away on 29-Jun-2019 with family at bedside. Immediate cause of death was reported as chronic hypoxemic respiratory failure. Autopsy details are unknown.

Deviations with potential medical significance: After the harvest of Omidubicel CF, it was determined that the TNC was 6.7 x 10e8 cells. Per the current version of the protocol approved at the site (Amendment IV), the TNC for the final Omidubicel CF must be >= 8.0 x 10e8 cells. The product met all other FPQC tests and release criteria. The FDA approved transplantation of this OOS product.

Subject Identifier	GP3DFC-007
Age	62
Sex	Male
Baseline Weight (Kg)	101.5
Race	White
Study Therapy	Mismatched Unrelated Donor
Date Of Study Therapy Administration	27 Nov 2018
Event	No SAEs reported
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	
Narrative: Patient GP3DFC-007 is a 62 year-old male with ALL who received a mismatched unrelated donor transplant on 27-Nov-2018.	

The patient was diagnosed with ALL on 28-Jun-2017. He underwent treatment with two cycles of induction E1910 therapy (Jul-2017). Consolidation therapy included one cycle of methotrexate (Oct-2017), one cycle intrathecal (IT) methotrexate and etoposide/cytarabine (Dec-2017), one cycle daunorubicin/vincristine and dex cytoxan, cytarabine, and 6MP (Jan-2018), and one cycle of cytarabine, etoposide, and IT-methotrexate/hydrocortisone (Mar-2018). Maintenance therapy included IT-methotrexate/vincristine, 6-MP, and methotrexate (Apr-2018) and reinduction therapy included three cycles of blinatumomab (May-2018) and one cycle of inotuzumab (Sep-2018). The patient's past medical history included mild hepatic impairment with hyperbilirubinemia at study screening.

On 16-Oct-2018, a BM exam confirmed remission status. However, MRD was found on flow cytometry which was still positive at a low level of 0.4%. The blasts were CD19 and CD22 negative at that time. Inotumuzmab dosing was therefore stopped. The decision was made to proceed with transplantation but given the exposure to inotumuzmab the treatment team opted not to pursue the cord blood transplant with myeloablative conditioning given the high-risk for VOD. Instead, the plan was to administer a reduced intensity conditioning regimen consisting of cyclophosphamide, fludarabine, and low dose TBI followed by the infusion of cells from a 10/12 HLA-mismatched donor. GvHD prophylaxis was given with post-transplantation cyclophosphamide, tacrolimus, and mycophenolate. Defibrotide was also planned as VOD prophylaxis. Neutrophil counts recovered at 15 days post-transplantation (12-Dec-2018). The patient was discharged from the hospital on 13-Dec-2018. The site reported no SAEs post-transplantation.

The site did not report all relapse events as SAEs, but since the protocol-defined relapse as a medically important event, the information has been provided.

A BM exam performed on 07-Aug-2019 revealed 66% blasts consistent with relapse of the patient's known ALL. Following relapse, the patient received two cycles of "mini" hyper-CVAD with inotuzumab. The patient underwent a subsequent SCT with an HLA-mismatched unrelated donor on 31-Oct-2019. As of the patient's final study-related visit on 02-Dec-2019, neutrophil counts had engrafted from the subsequent transplant and the disease was in complete remission.

Subject identifier	GP3DFC-008
Age	58
Sex	Female
Baseline weight (kg)	82.5
Race	White
Study therapy	Omidubicel
Date of study therapy administration	06 Mar 2019
Event	Acute Kidney Injury
Severity	Grade 3
Serious (yes/no)	Yes
Start/stop date of Event	08 May 2019 – 25 May 2019
Outcome of event	Resolved
Relationship to the study drug	No
Date of death (if applicable)	

Narrative:
Participant GP3DFC-008 is a 58 year-old White female with non-Hodgkin's Lymphoma who received an omidubicel transplant on 06-Mar-2019.

The participant was diagnosed with non-Hodgkin's Lymphoma (primary cutaneous CD30+ T-cell lymphoproliferative disorder) on 11-Apr-2012. The diagnostic biopsy showed a population of T-cells with a clonal T-cell receptor gamma chain gene rearrangement. Given suspicion for lymphomatoid papulosis, the participant was treated with methotrexate. This did not result in significant improvement. A PET scan at the time failed to show any evidence of systemic disease. Over the next few years, the participant received additional therapy including prednisone, narrow band UVB, PUVA therapy, brentuximab, and radiotherapy.

Stem cell transplantation was discussed but was not pursued at that time. The participant went on to receive romidepsin, reinduction with brentuximab, and PUVA and electron beam radiotherapy. She completed two cycles of therapy with pralatrexate. There was a reported increase in areas of new papules, therefore, the participant was enrolled in a clinical trial. She received treatment with duvelisib with excellent response. In early March 2018, the participant experienced marked progression of skin and blood disease, so she was started on alemtuzumab therapy. She received three cycles from 26-Mar-2018 to 17-Oct-2018. The participant's past medical history included cataract, dry eye, and pinguecula of both eyes. Surgical history included tonsillectomy (1964), laparoscopy (1999), and fertility surgery (2001). The participant had reported allergies to trimethoprim/sulfamethoxazole and cephalosporins.

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of thiotepa 324 mg/day (27-Feb-2019 to 28-Feb-2019), fludarabine 89.5 mg/day (01-Mar-2019 to 03-Mar-2019), and busulfan 226 mg/day (01-Mar-2019 to 03-Mar-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, acyclovir, diaminodiphenyl sulfone (Dapsome), valganciclovir, letermovir, and meropenum. Neutrophil counts recovered at eight days post-transplantation (14-Mar-2019). The participant was discharged from the hospital on 29-Mar-2019.

The participant presented for a regular clinic visit on 06-May-2019 where she was noted to have an elevated creatinine level of 2.62 mg/dL (baseline 0.9 mg/dL). She was treated with one liter of normal saline intravenously and her dose of tacrolimus was held since the level was supratherapeutic at 16 ng/mL. The participant's creatinine was reassessed on 08-May-2019 and it had increased to 3.11 mg/dL so she was admitted for management of acute kidney injury (AKI). A urinalysis on admission was unremarkable and other urine studies were most consistent with intrinsic AKI most likely caused by tacrolimus prior to admission. Tacrolimus was then restarted. Creatinine level on 10-May-2019 was 1.47 mg/dL. AKI continued to improve but the participant started to complain of epigastric pain. She was discharged with a plan to undergo an esophagogastroduodenoscopy (EGD) as an outpatient but was readmitted on 21-May-2019. The EGD was done on 23-May-2019. The participant was discharged again on 25-May-2019 with plans to follow up in clinic.

The participant had a single site of cutaneous recurrence on the right shoulder noted on 11-May-2020 confirming disease relapse. Radiation therapy was administered on 29-May-2020. The lesion completely resolved after the therapy.

Subject Identifier	GP3DFC-009
Age	57
Sex	Male
Baseline Weight (kg)	81.1
Race	White – North American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	05 Jul 2019
Event	1. AKI 2. Diarrhea
Severity	1. Grade 2 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 22 Jul 2019 – 29 Jul 2019 2. 18 Jan 2020 – 08 Feb 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	
Narrative:	

GP3DFC-009 is a 57 year-old White male with AML who received a Omidubicel transplant on 05-Jul-2019.

The patient was diagnosed with AML on 27-Dec-2018. He underwent treatment with one cycle of induction therapy with 7+3 (Cytarabine and Daunorubicin; 03-Jan-2019) and three cycles of consolidation therapy with HiDAC (14-Feb-2019). The patient's medical history included moderate/severe pulmonary impairment at study screening. He was a former smoker (2 packs per day x 10 years) and quit in Feb-2009.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (30-Jun-2019 to 02-Jul-2019), thiotepa (28-Jun-2019 to 29-Jun-2019), and busulfan (30-Jun-2019 to 02-Jul-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, trimethoprim-sulfamethoxazole, levofloxacin, and valacyclovir. Neutrophil counts recovered at 7 days post-transplantation (12-Jul-2019). The patient was discharged from the hospital on 17-Jul-2019.

The patient was admitted on 22-Jul-2019 for AKI management. He had a creatinine of 2.06 in the setting of decreased PO intake and was admitted for IV fluid and close electrolyte monitoring. On 23-Jul-2019 the patient had a new rash which covered <50% of his body surface area and diarrhea. He was started on prednisone for possible GvHD. The AKI was likely pre-renal (low fractional excretion of sodium (FeNA)) and improved with IV fluid and aggressive lactated ringers (LR). Flexible sigmoidoscopy done on 24-Jul-2019 showed normal morphology but GI Grade I GvHD was found on pathology on 25-Jul-2019. HHV6 viral load was also found to be high (>100k) on 24-Jul-2019. There was no evidence of encephalitis clinically. All stool infectious studies were negative. On 27-Jul-2019 the patient was transfused for epistaxis. On 28-Jul-2019 the HHV6 viral load was 1500. The AKI improved but did not return to baseline and on 29-Jul-2019 the patient was discharged home.

The patient was then admitted for diarrhea on 18-Jan-2020 with initial concerns of worsening GvHD. However, the patient had no further diarrhea on admission, even after his diet was advanced. He was discharged on 20-Jan-2020 on a regular BMT diet and resumed his prior dose of 80mg prednisone upon discharge. The diarrhea was considered likely a result of a food-born illness. The patient then returned to the ED on 01-Feb-2020 with worsening diarrhea over the previous several days since discharge. He reported having bowel movements up to 12 times per day with associated abdominal pain. He reported the bouts of diarrhea occurred following any oral intake but that he had continued eating and drinking to avoid dehydration. He was admitted for further workup and evaluation. A colonoscopy was performed on 03-Feb-2020 which revealed CMV colitis. The colitis and corresponding CMV viral load (max ~3500 copies/mL) responded to IV ganciclovir. The patient was discharged on oral Valcyte on 08-Feb-2020.

Subject Identifier	GP3DFC-010
Age	59
Sex	Female
Baseline Weight (Kg)	49.8
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	13 Dec 2019
Event	Febrile Neutropenia
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	04 Oct 2020 – 13 Oct 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	
Narrative: Patient GP3DFC-010 is a 59 year-old White female with acute lymphoblastic leukemia (ALL) who received a Omidubicel transplant on 13-Dec-2019.	

The patient was diagnosed with ALL on 15-Jul-2019. She underwent induction therapy with Larson I regimen starting on 22-Jul-2019 and intrathecal chemotherapy starting on 26-Aug-2019. Consolidation therapy included Larson Course IIA with intrathecal chemotherapy (13-Sep-2019), two cycles of intrathecal chemotherapy (Oct-2019), as well as vincristine and prednisone (12-Nov-2019). The patient's past medical history included Grover's disease, adjustment disorder, depression, anxiety, and moderate/severe hepatic impairment. She was noted to have cardiac impairment and moderate pulmonary impairment at study screening. The patient had reported allergies to penicillin, asparaginase, levofloxacin, and sulfasalazine.
Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (09-Dec-2019 to 12-Dec-2019), fludarabine (05-Dec-2019 to 07-Dec-2019), and cyclophosphamide (05-Dec-2019 to 06-Dec-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included trimethoprim-sulfamethoxazole and acyclovir. Neutrophil counts recovered at 7 days post-transplantation (20-Dec-2019). The patient was discharged from the hospital on 26-Jan-2020.
The patient presented to the Emergency Department on 04-Oct-2020 with worsening neutropenia and an ANC of 50 cells/µL. She reported a fever up to 100.7°F and chills while at home. The patient had visited the dentist on 24-Sep-2020 due to ongoing gum discomfort of unclear etiology. Since the dental visit, she reported having a sore throat, sore and swollen lymph nodes, dyspnea on exertion, occasional cough, increased nausea with abdominal cramping, and progressive fatigue. She denied urinary symptoms, rash, or chest pain. A chest X-ray demonstrated linear atelectasis and very subtle retrocardiac opacification. A CT scan of the head, chest, abdomen, and pelvis showed tonsillitis versus peritonsillar phlegmon and a peribronchial lesion in the right lung concerning for an underlying bacterial or fungal infection. COVID, parvovirus, adenovirus, CMV, EBV, influenza, and parainfluenza cultures were all negative. The ear nose and throat (ENT) service was consulted but decided it would not be possible to drain the phlegmon given the size of the fluid collection. The patient was treated with vancomycin (06-Oct-2020 to 09-Oct-2020), cefepime (04-Oct-2020 to 11-Oct-2020), metronidazole (05-Oct-2020 to 11-Oct-2020), and micafungin (09-Oct-2020 to 11-Oct-2020). A repeat CT scan performed on 09-Oct-2020 showed a multifocal pneumonia from aspiration versus community-acquired origin, likely revealed because of immune reconstitution as her ANC improved. A bronchoscopy was declined by the patient. On 11-Oct-2020 the patient's condition improved. Due to neutropenia, valganciclovir and trimethoprim-sulfamethoxazole were switched to letermovir/atovaquone. Filgrastim was also administered during the hospitalization. The patient was discharged on 13-Oct-2020 at which point the febrile neutropenia event was considered resolved. Upon discharge, the patient was instructed to complete a two-week course of amoxicillin through 22-Oct-2020.

Subject Identifier	GP3DUK-002
Age	44
Sex	Female
Baseline Weight (kg)	106.0
Race	Hispanic Filipino
Study Therapy	Not received
Date Of Study Therapy Administration	N/A
Event	1. Febrile Neutropenia 2. Relapsed AML
Severity	1. Grade 3 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 14 Apr 2017 – 01 May 2017 2. 16 Mar 2017 – 26 Jan 2018
Outcome Of Event	1. Resolved 2. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. NA: Pre-transplant event
Date Of Death (If Applicable)	26 Jan 2018
Narrative:	

Patient GP3DUK-002 is a 44 year-old Hispanic Filipino female with AML who consented to participate in the Omidubicel GP3 study on 20-Feb-2017. The patient did not receive the study transplant.

The patient was diagnosed with AML on 08-Mar-2016. She underwent treatment with one cycle of induction therapy with 7+3 (cytarabine and daunorubicin) following diagnosis in March 2016. She also received three cycles of consolidation therapy with HiDAC. Salvage chemotherapy was given on 22-Dec-2016 with MEC. The patient's past medical history included depression, diabetes, obesity, and systemic lupus erythematosus. She had cardiac impairment (ejection fraction of 50%) and severe pulmonary impairment (cDLCO = 54%) at study screening. No drug allergies were reported.

A BM biopsy was done on 16-Mar-2017 because the patient was still pancytopenic two months after completing MEC. The BM biopsy showed increased blasts at 5-10% by pathology and 8% by flow cytometry. The patient received six doses of cytarabine from 30-Mar-2017 to 04-Apr-2017. A repeat BM exam performed on 27-Apr-2017 showed 5-8% blasts which made the patient ineligible to proceed with the Omidubicel study transplant.

The patient underwent a BM exam on 01-Jun-2017 which showed 15% blasts, so she was enrolled in another clinical trial [Syros clinical trial: SY-1425-201 Ph2 (SY-1425 Tamibarotene AML-MDS)] on 01-Jun-2017. The patient was removed from the SY-1425-201 trial at the end of August 2017 due to a BM biopsy showing progressive disease with 20% blasts. The patient was then transferred back to her local primary team who started her on treatment with azacitidine.

On 30-Oct-2017, the clinical team informed the patient that her peripheral blast count was 3%, but her total WBC was only 0.7 x 10^9/L. She had completed two cycles of azacitidine and had febrile neutropenia at the time. The patient requested a BM aspiration test but was told a marrow would not be performed at that time. The patient refused hospice care.

The patient's death on 28-Jan-2018 was discovered through an obituary search. As the patient had a known history of relapse and failed multiple salvage treatments, the site investigator reported the primary cause of death as disease relapse/progression. No further details were available to site staff.

Subject Identifier	GP3DUK-003
Age	48
Sex	Male
Baseline Weight (kg)	78.9
Race	Black
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	03 May 2017
Event	1. Abnormal Echocardiogram 2. Relapsed AML
Severity	1. Grade 2 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 23 Mar 2017 – 24 Mar 2017 2. 09 Oct 2017 – 13 Dec 2017
Outcome Of Event	1. Resolved 2. Death
Relationship To The Study Drug	1. NA: Pre-Transplant Event 2. No
Date Of Death (If Applicable)	13 Dec 2017
Narrative: Patient GP3DUK-003 is a 48 year-old Black male with Acute Myelomonocytic Leukemia who received an Unmanipulated CBU transplant on 03-May-2017.	

The patient was diagnosed with Acute Myelomonocytic Leukemia (M4) on 18-Nov-2016. He was treated with standard 7+3 (daunorubicin 90 mg/m^2) on 19-Nov-2016 and began reinduction with HiDAC on 06-Dec-2016. He began HiDAC consolidation on 11-Jan-2017 and completed the third cycle on 13-Mar-2017. Other medical history included hypertension, history of hyperpigmentation on bilateral lower extremities due to lacerations suffered previously at work, and moderate pulmonary function - FEV1 78% and DLCO (uncorrected) 62%.

During routine pre-transplant evaluations on 23-Mar-2017, the patient's echocardiogram was suspicious for an IVC blood clot. He was admitted for further workup. A CT scan performed that evening ruled out an IVC blood clot. He was discharged in stable condition on 24-Mar-2017.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of nine sessions of TBI 150 cGy/dose (24-Apr-2017 to 28-Apr-2017), fludarabine 85 mg/day for 4 days (28-Apr-2017 to 01-May-2017), and thiotepa 445 mg/day for 2 days (22-Apr-2017 to 23-Apr-2017). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. He was on ciprofloxacin, voriconazole, dapsone, trimethoprim-sulfamethoxazole, pentamidine, piperacillin-tazobactam, vancomycin, micafungin, and acyclovir for infection prophylaxis. Neutrophil counts recovered at 25 days post-transplantation (28-May-2017). The patient was discharged from the hospital on 01-Jun-2017.

The patient's post-transplant course was complicated by CMV reactivation. He completed a course of valgancyclovir and was restarted on acyclovir for varicella zoster virus prophylaxis. Mycophenolate mofetil for GvHD prophylaxis was stopped on 17-Jul-2017. Tacrolimus was stopped on 11-Sep-2017 due to elevated creatinine and mycophenolate mofetil was then restarted as a substitute for the tacrolimus.

The patient was started on sorafenib on 26-Sep-2017. He developed diarrhea within one day of starting sorafenib and lost weight (9 pounds in one week). Stool exam showed yellow brown liquid with streaks of blood. Stool studies were negative for *C. diff.* The patient did not tolerate sorafenib and it was discontinued.

On 09-Oct-2017, a routine CBC differential showed 6% circulating blasts. A BM biopsy was done on 09-Oct-2017 and showed normocellular (60%) marrow with increased blasts (5-7%). The patient was diagnosed with relapsed acute myeloid leukemia on 09-Oct-2017. On 16-Oct-2017 the patient was found to have 20% circulating blasts and the decision was made to start him on MEC chemotherapy. The patient was admitted to the hospital for MEC chemotherapy from 23-Oct-2017 to 10-Nov-2017.

The patient was readmitted to the BMT service on 18-Nov-2017 for hypokalemia due to nausea, vomiting, and diarrhea in the setting of chemotherapy for relapsed AML. A manual differential from 19-Nov-2017 revealed 84% circulating blasts. The patient developed altered mental status overnight on 19-Nov-2017. He had a CT brain that was negative for a bleed. An MRI on 20-Nov-2017 revealed mild atrophy with no acute infarct. The patient was started on empiric thiamin and folic acid daily on 20-Nov-2017. His ammonia and thyroid stimulating hormone (TSH) levels were unremarkable. Blood cultures from 20-Nov-2017 were negative. The patient was found to have a positive CMV PCR (836 IU/ml) and was started on ganciclovir induction dosing on 20-Nov-2017.

After lengthy discussion with the patient, his family, and the primary BMT team regarding his terminal diagnosis, the patient was made DNR on 20-Nov-2017. The patient was transitioned to comfort care on 22-Nov-2017. He was sent home with local home hospice care on 05-Dec-2017. The patient's wife informed the site staff by telephone that the patient passed away on 13-Dec-2017. Autopsy was not performed. The primary cause of death was noted as disease relapse/progression/persistence.

Subject Identifier	GP3DUK-005
Age	44
Sex	Male
Baseline Weight (kg)	90.2
Race	Black - African American

Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	29 Nov 2017
Event	1. CO Diffusing Capacity Decreased 2. CMV Viremia
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 03 Nov 2017 – 07 Nov 2017 2. 28 Feb 2018 – 09 Mar 2018
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. NA: Pre-transplant event 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-005 is a 44 year-old Black, African American male with CML who received an Unmanipulated CBU transplant on 29-Nov-2017.

The patient was diagnosed with CML on 13-Nov-2000. He underwent induction therapy with interferon alfa (2000 – 2002) and three cycles of hyper-CVAD (Jul-2017 to Sep-2017), consolidation with two cycles of nilotinib (Sep-2017 to Oct-2017), and maintenance with Gleevec and Sprycel (2002-2017). The patient's past medical history included rectal fissure for 4 months in Oct-2010. He had steroid induced hyperglycemia and severe pulmonary impairment (cDLCO = 52% on 06-Oct-2017) at study screening.

The patient was initially admitted as scheduled on 03-Nov-2017 to start conditioning for a dual cord SCT. However, his PFTs were found to show a reduced DLCO. The patient underwent a repeat chest CT without contrast on 03-Nov-2017 which showed scattered nodular ground-glass opacities throughout the bilateral upper lobes, right middle lobe, and lingula, with associated bronchiectasis. The findings were concerning for multifocal endobronchial infection. The report also noted an 8x8 mm nodule on the left lower lobe of indeterminate cause, possibly infectious or postinfectious in origin. The decision was made to delay chemotherapy and SCT until infection could be ruled out by bronchoscopy. The patient underwent a bronchoscopy on 06-Nov-2017 with bronchoalveolar lavage. He tolerated it well. Since the patient did not have a ride home, he remained inpatient overnight after sedation for the procedure. The patient was discharged home on 07-Nov-2017 in stable condition.

The patient then received an Unmanipulated CBU transplant on 29-Nov-2017. Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (20-Nov-2017 to 24-Nov-2017), fludarabine (24-Nov-2017 to 27-Nov-2017), and thiotepa (18-Nov-2017 to 19-Nov-2017). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, ciprofloxacin, voriconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 22 days post-transplantation (21-Dec-2017). The patient was discharged from the hospital on 21-Dec-2017.

The patient was admitted on 28-Feb-2018 due to CMV viremia. He was started on IV ganciclovir 500 mg twice daily for ten days. He was then switched to twice daily oral valganciclovir after CMV titers were found to have decreased from 1827 to 945. The patient was discharged on 09-Mar-2018 to continue twice daily dosing of valganciclovir for two weeks or until his CMV DNA levels became undetectable at which point he was to continue once daily therapy.

Subject Identifier	GP3DUK-007
Age	46
Sex	Female
Baseline Weight (kg)	91.8
Race	Black
Study Therapy	Omidubicel
Date Of Study Therapy Administration	13 Dec 2017
Event	No events
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-007 is a 46 year-old Black female with Myelodysplastic Syndrome who received a Omidubicel transplant on 13-Dec-2017.

The patient was diagnosed with Myelodysplastic Syndrome (MDS) on 01-Aug-2017. She underwent treatment for MDS with Vidaza. The patient had moderate pulmonary impairment (DLCO 72%) at study screening. Her surgical history included hysterectomy (11-Apr-2013) and hernia repair (1973).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (04-Dec-2017 to 08-Dec-2017), fludarabine (08-Dec-2017 to 11-Dec-2017), and thiotepa (02-Dec-2017 to 03-Dec-2017). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, voriconazole, posaconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 14 days post-transplantation (27-Dec-2017). The patient was discharged from the hospital on 28-Dec-2017. The patient had no reported SAEs post-transplantation.

Subject Identifier	GP3DUK-008
Age	34
Sex	Male
Baseline Weight (kg)	135.1
Race	African American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	05 Sep 2018
Event	1. Fever 2. Septic Shock 3. GvHD 4. Aspiration Pneumonia 5. GI Symptoms
Severity	1. Grade 1 2. Grade 4 3. Grade 3 4. Grade 3 5. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 28 Sep 2018 – 30 Sep 2018 2. 08 Aug 2018 – 17 Aug 2018

	3. 30 Sep 2018 – 05 Oct 2018 4. 25 Oct 2018 – 31 Oct 2018 5. 13 Dec 2018 – 04 Jan 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Resolved
Relationship To The Study Drug	1. No 2. NA: Pre-Transplant Event 3. Yes 4. No 5. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-008 is a 34 year-old African American male with AML who received a Omidubicel transplant on 05-Sep-2018.

The patient was diagnosed with AML with abnormal BM eosinophils and inv(16) (p13;q22) or (t16;16) (p13;q22) (CBFb/MYH11) on 09-Feb-2017. His treatment included induction with 7+3 (09-Feb-2017) and 5+2 (24-Feb-2017), consolidation with HiDAC (cycle 1: 18-Apr-2017, cycle 2: 29-May-2017, cycle 3: 08-Jul-2017), reinduction with MEC (19-Feb-2018), reinduction with FLAG-Ida (11-Jun-2018), and consolidation with HiDAC (cycle 1: 23-Jul-2018). His past medical history included diabetes and obesity. He had moderate pulmonary impairment at screening.

The patient was admitted pre-transplant on 08-Aug-2018 for management of septic shock. The patient presented to the critical care unit (CCU) from the ED for septic shock with febrile neutropenia. Upon arrival to the ED, he was febrile at 103.8F, HR 127, RR 20, BP 131/57 and SpO2 100% on room air. He was started on cefepime and vancomycin, and received 4 L of IV fluids (2 NS, 2 LR). He became hypotensive with a blood pressure down to 78/36 with a lactate of 3.3 for which he was started on levophed drip. He was also started on IV micafungin for fungal coverage and was sent to the CCU. Blood culture was positive for gram-negative rods (GNR). He was continued on cefepime for GNR coverage. On 9-Aug-2018 he was weaned off the levophed drip after 8 liters of fluid and his lactate falling to 2.3.

The patient then developed watery diarrhea and his stool was found to be positive for C. difficile. Oral vancomycin was added and micafungin was stopped. On 10-Aug-2018, the patient had a fever. He was started on metronidazole. On 11-Aug-2018, the patient had poor urine output. His Hickman catheter was removed. However, the patient was still febrile. Blood cultures were repeated. On 12-Aug-2018, lovenox and IV vancomycin were discontinued while micafungin was restarted. The patient was still febrile and blood cultures were redrawn. He was then diagnosed with proctitis on CT chest/abdomen/pelvis. The patient was started on heparin drip, lasix 40 mg BID, and restarted on IV vancomycin.

On 14-Aug-2018 and 15-Aug-2018, the patient was still febrile. Blood cultures showed no growth to date. The patient was continued on vancomycin, cefepime, micafungin, and acyclovir. On 16-Aug-2018, the patient became afebrile and his blood cultures remained negative. His lasix was increased to 80mg BID. He was started on apixaban, and his IV vancomycin and heparin were discontinued. On 17-Aug-2018, a PICC line was placed, and the patient was discharged home, to follow-up in BMT clinic. The septic shock event was reported as resolved as of 17-Aug-2018.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (27-Aug-2018 to 31-Aug-2018), fludarabine 80 mg/day (31-Aug-2018 to 03-Sep-2018), and thiotepa 430 mg/day (25-Aug-2018 to 26-Aug-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included ciprofloxacin, acyclovir, Posaconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 15 days post-transplantation (20-Sep-2018). The patient was discharged from the hospital on 26-Sep-2018.

The patient was admitted for fever workup on 28-Sep-2018. He was started on empiric cefepime and vancomycin. Blood and urine cultures were negative. Chest x-ray did not show any focal opacities. On 30-Sep-2018, the patient had 3 L of stool output. Stool studies (cultures, C. diff, O&P) were negative. The patient was then evaluated on 30-Sep-2018 for GvHD. The patient had a flexible sigmoidoscopy on 01-Oct-2018 and EGD on 03-Oct-2018. As of 02-Oct-2018, the patient denied any changes in his bowel or bladder function. He continued to have significant loose bowel movements. On 03-Oct-2018, pathology from flexible sigmoidoscopy was negative for GvHD. Pathology showed occasional apoptotic bodies in the duodenum and stomach. Clinically, this was determined to be GvHD but given the improvements since admission, no active treatment for GvHD was initiated. The patient was briefly switched to IV mycophenolate and remained on IV tacrolimus at discharge. His HHV6 level was negative on 02-Oct-2018. Foscarnet was discontinued on 04-Oct-2018 and he was transitioned back to oral acyclovir on 04-Oct-2018. The patient's stool output was <1 L since 03-Oct-2018. He was clinically stable and discharged home on 05-Oct-2018.

The patient was then hospitalized from 25-Oct-2018 to 31-Oct-2018 for a lung infection. He then presented to the clinic on 13-Dec-2018 with a 2-day history of uncontrolled nausea, vomiting, and diarrhea. He was admitted for hydration, electrolyte support, and workup for GvHD vs infectious etiology. During the hospital course, the patient reported worsening of nausea, vomiting, and diarrhea. He denied fevers or chills but was weak and cold. He remained afebrile. C. Diff was negative from 15-Dec-2018. On 16-Dec-2018, the patient's abdominal pain worsened and he was placed on gut rest. Upper endoscopy and flexible sigmoidoscopy performed on 17-Dec-2018 showed no evidence of graft-versu- host disease. Budesonide was discontinued.

As of 20-Dec-2018, the patient continued with some diarrhea, nausea, and vomiting. He remained afebrile and continued to remain psychologically withdrawn. The patient was advanced to a regular diet. He denied nausea or vomiting, and the diarrhea became well controlled. The patient was discharged home from the hospital on 04-Jan-2019.

Subject Identifier	GP3DUK-009
Age	53
Sex	Male
Baseline Weight (kg)	58.7
Race	Black
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	22-Aug-2018
Event	1. Pulmonary Mucormycosis 2. AKI 3. Upper Respiratory Infection 4. Syncope 5. Gastrointestinal GvHD 6. Constipation
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3 5. Grade 3 6. Grade 2
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes 6. Yes
Start/stop date of Event	1. 20 Sep 2018 – 04 Oct 2018 2. 20 Oct 2018 – 19 Nov 2018 3. 08 Feb 2019 – 17 Mar 2019

	4. 11 May 2019 – 12 May 2019 5. 08 Feb 2019 – 19 Mar 2019 6. 07 Jun 2019 – 11 Jun 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Resolved 6. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No 5. Yes 6. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-009 is a 53 year-old Black male with AML who received an Unmanipulated CBU transplant on 22-Aug-2018.

The patient was diagnosed with AML (Acute myelomonocytic leukemia – M4) on 27-Feb-2017. His treatment included induction 7+3 with daunorubicin 90 mg/m^2 and cytarabine 100 mg/m^2 (03-Mar-2017), consolidation with HiDAC cycle 1 (10-Apr-2017), HiDAC cycle 2 (20-May-2017), and HiDAC cycle 3 (20-Jun-2017), reinduction with 7+3 and gemtuzumab (18-Apr-2018), and consolidation with HiDAC cycle 1 (16-Jun-2018). His past medical history included enterocolitis with partial small bowel occlusion in Apr-2018. Surgical history included bronchoscopy (03-May-2017) and right upper lobe wedge resection (09-May-2017). He had severe pulmonary impairment at screening (FEV1 of 65% on PFTs 02-Jul-2018). He was antibody positive for VZV, EBV IgG, and CMV antibodies at screening. He also had a reported allergy to posaconazole.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (13-Aug-2018 to 17-Aug-2018), fludarabine 80 mg/day (17-Aug-2018 to 20-Aug-2018), and thiotepa 400 mg/day (11-Aug-2018 to 12-Aug-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Neutrophil counts recovered at 17 days post-transplantation (08-Sep-2018). The patient was discharged from the transplant hospitalization on 17-Oct-2018.

The patient was hospitalized for mucormycosis from 20-Sep-2018 to 04-Oct-2018, AKI from 20-Oct-2018 to 19-Nov-2018, and upper respiratory infection from 08-Feb-2019 to 17-Mar-2019. The patient was primarily admitted to the hospital on 08-Feb-2019 for worsening cough, congestion, and progressive failure to thrive. He was afebrile. He had previously endorsed nausea and diarrhea. Stool cultures and viral electron microscopy were negative. However, he was found to be C. difficile positive on admission. He was started on Dificid on 09-Feb-2019 due to intolerance to oral vancomycin. He had significant sputum production and weight loss. Fungal, viral serum, and respiratory cultures were negative. Blood cultures were also negative. A chest CT revealed peribronchial ground-glass opacities and a cavitary right apical pulmonary nodule with increased soft tissue components concerning for multifocal infection. A CT of his sinuses revealed increased maxillary sinus disease. He was started on cefepime. Doxycycline was added from 10-Feb-2019 to 16-Feb-2019 after consultation with ID. Pulmonology was consulted for bronchoscopy. However, the bronchoscopy was withheld given clinical improvement with antibiotics and symptom management. Cefepime was then discontinued on 13-Feb-2019.

The patient continued to have progressive weight loss and decreased oral intake secondary to nausea and vomiting. An EGD on 11-Feb-2019 revealed GvHD in his stomach and duodenum. On admission, the patient's tacrolimus level was undetectable, and he admitted to no longer taking the medication. Tacrolimus was restarted as an IV medication. In discussion with his primary BMT physician, he was started on Solumedrol 0.5 mg/kg/day on 12-Feb-2019 and it was increased to 1 mg/kg/day on 16-Feb-2019. He was started on TPN on 16-Feb-2019. The patient developed evidence of hemolysis on labs with decreased haptoglobin and LDH trending up starting 17-Feb-2019. Tacrolimus was discontinued on 20-Feb-2019. Peripheral flow cytometry

was negative for blasts but did show microangiopathic hemolytic anemia. ADAMTS13 gene activity was shown as slightly decreased at 57% on 21-Feb-2019. His GvHD symptoms improved, so Solumedrol was decreased to 40 mg daily on 24-Feb-2019 and changed to equivalent PO prednisone 50mg daily on 03-Mar-2019.

The patient continued to hemolyze, so he received IVIG x 5 days from 25-Feb-2019 to 01-Mar-2019, with a plan to add Rituxan if there was no improvement. He started mycophenolate mofetil 1 g BID on 01-Mar-2019 for GvHD in the setting of discontinued tacrolimus and weaning steroids. Jakafi 5mg every other day was started on 08-Mar-2019 (dose due to interaction with Posaconazole). Surveillance screening found the patient to be CMV positive on 07-Mar-2019 (403 IU/ml) with follow-up of 480 IU/ml on 11-Mar-2019. The patient was started on induction ganciclovir on 08-Mar-2019 with transition to PO valcyte on 13-Mar-2019. Prednisone was decreased to 30 mg daily on 13-Mar-2019. The patient's liver enzymes as well as LDH appeared to be up trending on 14-Mar-2019. Given concern for liver GvHD, the patient underwent a transjugular liver biopsy on 15-Mar-2019. By the time of discharge, the patient was eating and drinking well. He continued to have soft bowel movements. He denied any shortness of breath, cough, or chest pain. The patient was discharged on 17-Mar-2019.

The patient had a follow-up visit on 19-Mar-2019. The patient reported increased appetite, weight gain, and formed stools since his discharge. He denied any abdominal cramping or fevers. The gastrointestinal GvHD event was reported as resolved as of 19-Mar-2019.

Subject Identifier	GP3DUK-010
Age	20
Sex	Male
Baseline Weight (kg)	78.9
Race	Multiracial - Asian, Caucasian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	12 Sep 2018
Event	PGF
Severity	Grade 4
Serious (Yes/no)	Yes
Start/stop date of Event	23 Oct 2018 – 05 Nov 2018
Outcome Of Event	Resolved
Relationship To The Study Drug	Yes
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-010 is a 20 year-old multiracial (Asian, Caucasian) male with AML who received an Unmanipulated CBU transplant on 12-Sep-2018.

The patient was diagnosed with AML (Acute Myelomonocytic Leukemia – M4) on 29-May-2018. He underwent 7+3 induction therapy starting on 30-May-2018, consolidation with HiDAC, and reinduction with FLAG-IDA on 05-Jul-2018. Past medical history included cardiac history (LVEF 50%) and moderate pulmonary impairment. He had a history of atrial fibrillation (20-Jul-2018 A-fib with rapid ventricular rate (RVR) controlled by metoprolol) that was absent at study screening. Past surgical history included appendectomy in 2006.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (03-Sep-2018 to 07-Sep-2018), fludarabine 80 mg/day (07-Sep-2018 to 10-Sep-2018), and thiotepa 400 mg/day (01-Sep-2018 to 02-Sep-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, ciprofloxacin, and trimethoprim-sulfamethoxazole.

The patient received the Unmanipulated CBU transplant on 12-Sep-2018. The post-transplantation period was complicated by persistent neutropenic fevers. Initial infectious workup was negative. The patient showed no

engraftment following study transplant. WBC initially came up to 0.4 on 30-Sep-2018 and then trended back down to 0.1 on 03-Oct-2018. The patient had a BM biopsy on 04-Oct-2018 which showed a variably hypocellular marrow (<5-50%) with focal left shift, trilineage maturation, and no evidence of blasts. FISH was negative. Whole blood peripheral engraftment studies on 05-Oct-2018 showed 70% donor cells. Granix dose was increased on 06-Oct-2018.

A repeat BM biopsy was done on 17-Oct-2018 and showed a markedly hypocellular marrow (<5%) with decreased to absent hematopoiesis and no blasts. Peripheral blood WBC was <0.1. The patient was diagnosed with PGF on 17-Oct-2018 by BM examination. The site investigator considered this to be PGF by protocol definition on 23-Oct-2018 (post-transplantation day +42). The study site proceeded to treat the patient with a haploidentical transplant (mother). The patient received conditioning regimen with fludarabine, cyclophosphamide, and Campath on 24-Oct-2018 and TBI on 25-Oct-2018 prior to reinfusion. The patient received the haploidentical SCT on 25-Oct-2018. He engrafted with ANC >1000 as of 05-Nov-2018. The patient was stable and discharged from the hospital on 12-Nov-2018.

Subject Identifier	GP3DUK-012
Age	38
Sex	Male
Baseline Weight (kg)	108.6
Race	Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	01 May 2019
Event	1. Hyperglycemia 2. Pneumonia 3. Bronchospasm
Severity	1. Grade 3 2. Grade 3 3. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 04 Jun 2019 – 05 Jun 2019 2. 08 Jan 2020 – 13 Jan 2020 3. 03 Dec 2019 – 04 Dec 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-012 is a 38 year-old Asian male with AML who received an Unmanipulated CBU transplant on 01-May-2019.

The patient was diagnosed with AML on 10-Dec-2018. He underwent induction therapy with 7+3 (Cytarabine and Idarubicin; 21-Dec-2018) and salvage therapy with MEC (mitoxantrone, etoposide, cytarabine; 09-Feb-2019). The patient's past medical history also included myelocytic sarcoma on the right chest wall, asthma, obesity (BMI = 36.3 kg/m^2), eczema, gout, Graves' disease (treated with radioactive iodine in 2006), hypothyroidism (post-RDI), hemorrhoids, and hypertension. He was treated for bacteremia due to vancomycin-resistant Enterococcus in Jan-2019. He had moderate/severe pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (22-Apr-2019 to 26-Apr-2019), fludarabine (26-Apr-2019 to 29-Apr-2019), and thiotepa

(20-Apr-2019 to 21-Apr-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. The tacrolimus was switched to cyclosporine on visit day +28. Infection prophylaxis included acyclovir, ciprofloxacin, posaconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 19 days post-transplantation (20-May-2019). The patient was discharged from the hospital on 03-Jun-2019.

On 04-Jun-2019, the patient's caregiver reported that the patient had a blood glucose level of 583, with a re-check level of 586. The caregiver was instructed to give the patient 12 units of Lispro Insulin and re-check in one hour. The patient's blood glucose remained above 500 after 12 units of Lispro Insulin. The patient was instructed to come to the hospital and was admitted for observation, IV fluids, and monitoring of blood glucose. By midnight, the patient's blood glucose was down to 188 and was 92 by breakfast. The patient was counseled to limit concentrated sweets in his diet and was discharged on 05-Jun-2019. Given his concurrent steroid taper, no adjustments were made to the patient's insulin regimen.

The patient was then admitted on 03-Dec-2019 for observation after excisional lymph node biopsy by ENT. The patient began to have bronchospasm and needed oxygen support after the biopsy procedure. The patient was treated with albuterol nebs given his significant history of asthma which reduced his symptoms. By the time he had reached the ABMT team he was stable on room air. On 04-Dec-2019 the patient was stable and discharged back to the ABMT clinic team.

On 08-Jan-2020 the patient was admitted for management of pneumonia. The patient had reported a worsening, dry cough with some white sputum over the prior few weeks and had recently developed pleuritic pain. He denied any recent sick contacts or other URI symptoms. He had been using albuterol and nebulizers at home with some temporary relief. A chest CT found interval development of bilateral centrilobular nodules and peribronchial ground-glass opacities, concerning for multifocal endobronchial infection, and a slight increase in a small pericardial effusion. He was admitted on 08-Jan-2020 for further evaluation of the abnormal chest CT.

The patient had a persistent, mostly dry cough on 09-Jan-2020. He also continued to endorse poor sleep due to the dry cough but reported some relief with increase in nebulizer treatments. On 10-Jan-2020 the patient underwent a bronchoscopy without complications. He continued to have a dry cough that improved with Duonebs and codeine. On 13-Jan-2020 the patient was feeling better despite a continuing irritating cough. Given clinical improvement with scheduled nebulizer treatments and ribavirin the patient was discharged on 13-Jan-2020.

Subject Identifier	GP3DUK-014
Age	56
Sex	Female
Baseline Weight (kg)	65.2
Race	Black
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	06 Jun 2019
Event	1. Febrile Neutropenia 2. Septic Shock 3. Gastrointestinal GvHD 4. Disease Progression/Relapse
Severity	1. Grade 3 2. Grade 4 3. Grade 3 4. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 15 May 2019 – 19 May 2019

	2. 04 Jul 2019 – 08 Jul 2019 3. 05 Jul 2019 – 26 Jul 2019 4. 16 Jul 2019 – 26 Jul 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Death 4. Death
Relationship To The Study Drug	1. NA: Pre-transplant Event 2. No 3. Yes 4. No
Date Of Death (If Applicable)	26 Jul 2019

Narrative:
Patient GP3DUK-014 is a 56 year-old Black female with AML who received an unmanipulated CBU transplant on 06-Jun-2019.

The patient was diagnosed with AML on 18-Nov-2016. She was treated with induction 7+3 regimen, consolidation with four cycles of HiDAC (16-Jan-2017 to 22-Apr-2017), and reinduction with three cycles Azacytidine and Venetoclax (12-Jan-2019 to May-2019). Past medical history included central diabetes insipidus. The patient had reported allergies to penicillin and vancomycin.

Prior to unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (28-May-2019 to 01-Jun-2019), fludarabine 65 mg/day (01-Jun-2019 to 04-Jun-2019), and thiotepa 295 mg/day (26-May-2019 to 27-May-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Neutrophil counts recovered at 13 days post-transplantation (19-Jun-2019). The patient was discharged from the hospital on 24-Jun-2019.

The patient was initially admitted from the daily ABMT clinic on 04-Jul-2019 for significant dehydration and hypotension that was fluid responsive. She reported nausea, vomiting, and diarrhea that had been persistent for four days and she had missed most of her medication doses during that time. She denied any chest pain, cough, or shortness of breath. She was afebrile. There was no history of new skin rashes or lesions. She appeared fatigued. At 1800 on 04-Jul-2019, the patient reported dizziness and difficulty ambulating to the bathroom. The patient then appeared more lethargic and was noted to have chills (Temp 99.6, HR at 160, BP 90s/50s). The MICU was consulted, blood cultures drawn, and the patient was started on cefepime, Flagyl, and Vancomycin. The patient received 1 L LR bolus with minimal improvement of blood pressures. She had a lactate of 5.7, creatinine of 1.3 up from a baseline of 0.6-0.7, and a blood gas of 7.4/1/20/82. Vitals were HR 150s, Temp 102.7, and BP ranging from 60-70s. The patient was also noted to be tachypneic with saturations of 90-100% on room air. Given worsening clinical condition and acute findings, the patient was transferred to the MICU on 04-Jul-2019 for blood pressure support and septic shock management.

In the MICU the patient received norepinephrine, vasopressin, and two 200 mcg boluses of phenylephrine. A total of approximately 4 L of intravenous fluids were given along with pressor support, and her blood pressures began to normalize. During her stay in the MICU, the patient was intermittently hypotensive requiring continued pressor support. The hypotension was ultimately attributed to massive GI losses secondary to refractory diarrhea. With concern for possible GvHD, an EGD with biopsy was done on 05-Jul-2019. Imodium was started to decrease the frequency of bowel movements. Intermittent GI discomfort was treated with GI cocktail, simethicone, and oxycodone as needed. The patient showed improvements with Imodium and GI cocktail. EGD and flexible sigmoidoscopy biopsies were positive for GvHD. The patient was diagnosed as having GI GvHD on 05-Jul-2019.

The patient was started on Solumedrol 1 mg/kg on 06-Jul-2019. Blood cultures were reported as negative. Antibiotics were changed to meropenem on 06-Jul-2019. The patient was transferred back to the transplant floor on 08-Jul-2019. Septic shock was reported as resolved as of 08-Jul-2019. The patient's diarrhea improved with increasing Imodium dosing. She continued to have intermittent abdominal cramping and some nausea, but no vomiting. The patient remained stable and afebrile but continued to endorse fatigue. She remained on TPN for nutritional support.

On 13-Jul-2019, the patient was found to have a CBC with differential showing 10% blasts in the blood. By 16-Jul-2019, the blasts had increased to 32%. On 16-Jul-2019, peripheral blood flow cytometry confirmed disease relapse with 35% phenotypically abnormal myeloid blasts. The patient was diagnosed as having disease progression/relapse on 16-Jul-2019. The patient was started on hydrea and decitabine on 19-Jul-2019. On 22-Jul-2019, the patient refused further treatment and requested to be discharged home to family. Active treatment for AML was discontinued and the patient was discharged from hospital to inpatient hospice on 23-Jul-2019. The patient died at her local hospice facility on 26-Jul-2019. Autopsy was not done. Primary cause of death was noted as disease progression/relapse.

Subject Identifier	GP3DUK-015
Age	19
Sex	Female
Baseline Weight (kg)	90.3
Race	Black - African American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	18 Sep 2019
Event	1. Fever 2. GI GvHD 3. Hyperglycemia 4. Anxiety 5. Secondary Graft Failure 6. *C. Difficile* Colitis
Severity	1. Grade 1 2. Grade 3 3. Grade 3 4. Grade 3 5. Grade 3 6. Grade 2
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes 6. Yes
Start/stop date of Event	1. 17 Nov 2019 – 22 Nov 2019 2. 29 Nov 2019 – 05 Dec 2019 3. 10 Dec 2019 – 11 Dec 2019 4. 25 Jan 2019 – 27 Jan 2019 5. 05 Mar 2020 – 21 Apr 2020 6. 11 Aug 2019 – 20 Aug 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved with sequelae 5. Resolved 6. Resolved
Relationship To The Study Drug	1. No 2. Yes 3. No 4. No 5. No 6. NA: Pre-transplant event
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-015 is a 19-year-old Black, African American female with ALL who received a Omidubicel transplant on 18-Sep-2019.

The patient was diagnosed with ALL (BCR/ABL+ ALL) on 01-Apr-2019. On 04-Apr-2019 she started induction therapy with cycle 1 of protocol CALGB 8811 with dasatinib. On 01-May-2019 the patient achieved complete remission. On 08-May-2019 she started part B hyper-CVAD and on 05-Jun-2019 she started part A R-Hyper-CVAD. Bone marrow biopsy on 03-Jul-2019 was negative for disease. The patient was then restarted on dasatinib on 03-Jul-2019 but it was discontinued on 11-Aug-2019. The patient was treated for *Clostridium difficile* colitis from 11-Aug-2019 to 20-Aug-2019. The patient's past medical history included obesity (BMI = 37.09 kg/m^2).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (09-Sep-2019 to 13-Sep-2019), fludarabine 65 mg/day (13-Sep-2019 to 16-Sep-2019), and thiotepa 290 mg/day (07-Sep-2019 to 08-Sep-2019). GvHD prophylaxis included mycophenolate mofetil and both tacrolimus and cyclosporine due to tacrolimus intolerance. Infection prophylaxis included acyclovir, voriconazole, posaconazole, micafungin, trimethoprim-sulfamethoxazole, and vancomycin. Neutrophil counts recovered at eight days post-transplantation (26-Sep-2019). The patient was discharged from the hospital on 07-Oct-2019.

The patient presented to the ED with a fever of 100.4°F on 17-Nov-2019. This was the first time she had a fever since her transplant. The patient endorsed about two days of a productive cough with clear sputum and positive sick contacts who also had coughs. She also noted abdominal pain. A CT scan of the chest/abdomen/pelvis found a thickened urinary bladder wall possibly related to decompression and incidentally noted a left portal vein aneurysm stable from prior exam. The patient was treated with daptomycin until 20-Nov-2020 and piperacillin-tazobactam until 21-Nov-2019. She remained afebrile and was transitioned back to prophylactic ciprofloxacin on 21-Nov-2019. The patient was discharged in stable condition on 22-Nov-2019.

The patient was then seen in outpatient clinic on 29-Nov-2019 for follow-up of failure to thrive. During assessment, the patient reported a history of anorexia, persistent nausea without vomiting, and fatigue. She denied diarrhea, constipation, abdominal pain, or cramping. The patient was noted to have a 4 kg weight loss since 20-Nov-2019. The patient had started taking budesonide 3 mg three times a day on 27-Nov-2019 with no reported improvement. She was admitted on 29-Nov-2019 for concerns and evaluation of GI GvHD.

On admission the patient was started on intravenous fluids and methylprednisolone at 1 mg/kg per day. Budesonide was continued. The patient underwent an esophagogastroduodenoscopy and flexible sigmoidoscopy on 02-Dec-2019. Pathology from the procedure was consistent with likely GvHD of the duodenum and possible GvHD of the stomach. The patient reported significant appetite and nausea improvement with fluids and steroids and was able to be discharged home on 05-Dec-2019. The plan was to taper methylprednisolone as tolerated.

The patient was then found to have blood sugars in the 300s-400s on 10-Dec-2019. She had been receiving insulin glargine injections in clinic but admitted to being non-compliant with a diabetic-type diet. She received 5 units of insulin lispro on admission and was started on sliding scale insulin with improvement of blood glucose levels. On 11-Dec-2019 a diabetes educator and dietitian were consulted and provided education to the patient regarding insulin administration and how to monitor blood glucose. Blood sugars down trended to the 180s-250s and the patient was discharged home on 11-Dec-2019.

On 25-Dec-2019 the patient was admitted due to concerns by the patient and her caregiver (mother) that she was not taking her medications correctly. The patient reported feeling dizzy and "fuzzy-headed" which she believed started after starting insulin. She also felt that her recently started escitalopram was having no effect. She complained of occasional abdominal pain, back pain, mild frontal headache, and recent cough and diarrhea. She reported not eating as much as she should be but denied nausea or vomiting. The patient was discharged home on 27-Dec-2019. A home health was set up to assist with medication management and a new prescription for mirtazapine was given to help with anxiety and depression.

The patient then presented to an outside hospital ED with a complaint of headaches on 05-Mar-2020. Of note, cyclosporine was changed to tacrolimus in Sep-2019 due to complaints of chronic headaches. Complete blood counts revealed the patient to be pancytopenic with a normal complete metabolic panel. A CT of the head was negative for abnormalities. A flu panel was negative. The patient was transferred to the study site and dasatinib was held upon admission.

On 06-Mar-2020, the patient underwent a BM biopsy and aspirate which indicated disease relapse. The patient was diagnosed with secondary graft failure on 06-Mar-2020. Results showed BCR/ABL negative, flow positive, 8% precursor B cells with features consistent with hematogones. Pathology showed 50% cellular BM with hematogones with decreased trilineage hematopoiesis. HHV6 was detected at <183 copies/mL in the BM, but there were negative HHV6 peripheral studies on 05-Mar-2020. On 11-Mar-2020, a lumbar puncture was performed to rule out disease versus infection and was found to be negative.

Given BM findings and engraftment studies revealing CD3 24%, CD15 >98%, and whole blood 95%, the patient was given one dose of intravenous immunoglobulin 1 g/kg and four doses of dexamethasone 40 mg by mouth. On 18-Mar-2020, cyclosporine was discontinued. On 25-Mar-2020, viral studies, fungal cultures, and BCR/ABL were negative. Repeat BM studies and flow revealed markedly to absent myeloid and erythroid precursors. Pathology showed 5-10% hypocellular marrow.

Following a conditioning regimen consisting of fludarabine, cyclophosphamide, and TBI, the patient received a second transplant from a haploidentical donor on 07-Apr-2020. Neutrophil engraftment was achieved on 21-Apr-2020.

Subject Identifier	GP3DUK-016
Age	51
Sex	Female
Baseline Weight (kg)	48.6
Race	Hispanic or Latino
Study Therapy	Omidubicel
Date Of Study Therapy Administration	16 Oct 2019
Event	1. Hypernatremia 2. Septic Shock 3. GI GvHD
Severity	1. Grade 1 2. Grade 4 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 08 Dec 2019 – 08 Jan 2020 2. 02 Jan 2020 – 03 Jan 2020 3. 30 Oct 2019 – 16 Jan 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Death
Relationship To The Study Drug	1. No 2. No 3. Yes
Date Of Death (If Applicable)	16 Jan 2020
Narrative: Patient GP3DUK-016 is a 51 year-old Hispanic or Latino female with Non-Hodgkin Lymphoma who received a Omidubicel transplant on 16-Oct-2019.	

The patient was diagnosed with Non-Hodgkin Lymphoma (Angioimmunoblastic T-cell Lymphoma) on 15-Oct-2018. She underwent treatment with six cycles of CHOEP (cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone) from 28-Nov-2018 to 12-Mar-2019. On 16-Apr-2019 a BM biopsy showed atypical but non-clonal B cells and no T-cell lymphoma. On 31-May-2019, PET/CT scan showed recurrence of disease with interval increase in size and number of hypermetabolic lymphadenopathies above and below the diaphragm consistent with disease recurrence. The patient then underwent treatment with five cycles of Belinostat from 17-Jun-2019 to 09-Sep-2019. PET/CT scan on 29-Aug-2019 demonstrated complete response. The patient's past medical history also included hypothyroidism, chemotherapy-induced cardiomyopathy (EF 40% in Nov-2019), anxiety, panic disorder, and PE. She had moderate pulmonary impairment at study screening (cDLCO = 57%). She had reported allergies to allopurinol, azithromycin, chlorhexidine gluconate, and Levaquin. She also had a history of sensitivity to vancomycin.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (07-Oct-2019 to 11-Oct-2019), fludarabine 55 mg/day (11-Oct-2019 to 14-Oct-2019), and thiotepa 250 mg/day (05-Oct-2019 to 06-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, ciprofloxacin, posaconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at nine days post-transplantation (25-Oct-2019).

The post-transplantation hospital course was complicated by mucositis, esophagitis, and febrile neutropenia. During WBC recovery, the patient had increased nausea, vomiting, and diarrhea. The patient underwent a CT scan of the abdomen and pelvis on 28-Oct-2019 which showed no acute findings. An esophagogastroduodenoscopy was performed on 30-Oct-2019 which showed multiple apoptotic bodies and possible GvHD was noted. Solumedrol 2 mg/kg daily was started on 02-Nov-2019. Due to continued poor intake, nausea, and vomiting, Jakafi 5mg twice a day was started on 15-Nov-2019 and increased to 10 mg twice a day on 22-Nov-2019. Due to neurologic symptoms tacrolimus was switched to cyclosporine on 21-Nov-2019. The patient's stool output and abdominal pain improved as of 02-Dec-2019 and the patient was able to be discharged on 05-Dec-2019.

On 08-Dec-2019, the patient was readmitted with hypernatremia, secondary to dehydration from her persistent and significant diarrhea, and resolving HHV6 viremia. The patient complained of intermittent abdominal pain as well. Lab values revealed significant lactic acidosis with a lactate of 9.7. Other lab values of note included a potassium of 7.5, BUN of 102, and a creatine of 1.3. The patient was transferred to the MICU for close monitoring. She was given one liter of albumin, one liter of normal saline, and was started on a bicarbonate drip. She also required a norepinephrine drip for blood pressures in the 70s/50s. Blood cultures and urinalysis were obtained. Antimicrobial coverage included cefepime, flagyl, micafungin, and daptomycin. Arterial blood gases were checked every two hours.

A CT of the abdomen and pelvis showed non-specific enterocolitis. Stool output at admission averaged one liter per day. The patient was continued on Cellcept, cyclosporine, Jakafi, and solumedrol. Due to altered mental status, there was a concern of a CNS infection. An MRI of the brain showed no new abnormalities. Given past HHV6 viremia, the patient was also started on ganciclovir. While in the ICU, the patient required emergent CRRT to correct electrolyte abnormalities, which was stopped soon after, as electrolytes rapidly corrected. The patient's mental status improved.

On 24-Dec-2019, the patient was started on budesonide in order to taper systemic steroids. On 29-Dec-2019, HHV6 levels were < 188 copies/mL. On 31-Dec-2019, a CT of the abdomen and pelvis found prominent loops of fluid filled colon with diffusely increased small bowel wall enhancement and mild thickening. The patient was then placed on bowel rest and started on Zosyn.

On 01-Jan-2020, the patient declined clinically. She had increased confusion, anxiety, hypothermia, and hypotension. She was transferred to the MICU for close monitoring of septic shock. CT scan of the abdomen and pelvis on 02-Jan-2020 did not show an abscess or perforation. On 03-Jan-2020, Solumedrol was increased to 2 mg/kg/day, tocilizumab was added, and Jakafi was held. On 05-Jan-2020, lactate was down to 2.5 and the patient was transferred back to the BMT unit for continuation of inpatient care.

The patient continued to have frequent watery diarrhea. Her stools became profoundly bloody and the patient required daily transfusion support with packed RBC, platelets, and cryoprecipitate. Given her immunosuppression and clinical symptoms, a repeat flexible sigmoidoscopy was performed on 06-Jan-2020 to evaluate for infection vs GvHD. The pathology was unremarkable; however, biopsies were limited to distal exam only. On 09-Jan-2020, a lumbar puncture was negative for HHV6.

The patient continued to decline despite aggressive therapies. With the lack of response to GvHD medications and likelihood that the patient would not recover, the family agreed to transition the patient to 'comfort care only' on 10-Jan-2020. Octreotide 100 mcg every 8 hours and Dilaudid infusion for pain control were started, with improvement of diarrhea. The patient passed away on 16-Jan-2020. The primary cause of death was noted as GvHD, with secondary cause noted as sepsis. Autopsy was performed at the request of the family. Autopsy report on 13-May-2020 revealed no evidence of disease recurrence.

Subject Identifier	GP3DUK-017
Age	38
Sex	Male
Baseline Weight (kg)	91.4
Race	Unknown
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	02 Oct 2019
Event	RSV Infection
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	17 Jan 2020 – 21 Jan 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3DUK-017 is a 38-year-old male with AML who received an unmanipulated CBU transplant on 02-Oct-2019.

The patient was diagnosed with AML on 13-May-2019. He underwent induction therapy with 7+3 and midostaurin (May-2019) and consolidation therapy with four cycles of HiDAC and midostaurin (Jun-2019 to Sep-2019). The patient's past medical history included hypertension. He had moderate pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (23-Sep-2019 to 27-Sep-2019), fludarabine (27-Sep-2019 to 30-Sep-2019), and thiotepa (21-Sep-2019 to 22-Sep-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included valganciclovir, posaconazole, and ciprofloxacin. Neutrophil counts recovered at 20 days post-transplantation (22-Oct-2019). The patient was discharged from the hospital on 31-Oct-2019.

The patient was admitted for RSV infection on 17-Jan-2020. He was started on ribavirin and palivizumab. A non-contrast chest CT scan was negative for pneumonia. The patient was stable on 20-Jan-2020 and discharged home.

Subject Identifier	GP3DUK-018
Age	51
Sex	Male
Baseline Weight (kg)	78.6
Race	Black – African American
Study Therapy	Omidubicel

Date Of Study Therapy Administration	30 Oct 2019
Event	1. GI GvHD 2. HHV6 Encephalitis
Severity	1. Grade 5 2. Grade 4
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 14 Nov 2019 – 30 Dec 2019 2. 18 Nov 2019 – 30 Dec 2019
Outcome Of Event	1. Death 2. Death
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	30 Dec 2019

Narrative:
Patient GP3DUK-018 is a 51 year-old Black, African American male with AML who received a Omidubicel transplant on 30-Oct-2019.

The patient was diagnosed with AML on 25-Feb-2019. He received 7+3 induction chemotherapy in March 2019. The patient then underwent consolidation therapy with seven cycles of Dacogen with Venetoclax from Mar-2019 to Sep-2019. The patient's past medical history included severe pulmonary impairment which was present at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (21-Oct-2019 to 25-Oct-2019), fludarabine 85 mg/day (25-Oct-2019 to 28-Oct-2019), and thiotepa 460 mg/day (19-Oct-2019 to 20-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, levofloxacin, posaconazole, pipercillin-tazobactam, and micafungin. Neutrophil counts recovered at 12 days post-transplantation (11-Nov-2019).

The patient's post-transplantation hospital course was complicated by S. Mitis bacteremia (treated with cefepime and vancomycin; 31-Oct-2019), pancytopenia, and neutropenic fever (07-Nov-2019). The patient was also noted to have increased stool output post-transplantation. On 14-Nov-2019, the patient underwent an esophagogastroduodenoscopy (EGD) and flexible sigmoidoscopy. Biopsies obtained during the procedure were noted to have markedly increased epithelial apoptosis. The patient was diagnosed with GI GvHD on 14-Nov-2019. The patient was started on Solumedrol 2 mg/kg/day. On 18-Nov-2019, the patient was given one dose of octreotide. Tocilizumab was also started, with dosing every 14 days. The patient received a total of three doses of tocilizumab.

On 18-Nov-2019, the patient began having seizures. He was transferred to the CCU and intubated for airway protection. The seizures were initially controlled by intravenous Ativan. The patient was extubated on 20-Nov-2019. MRI of the brain and CT of the head were negative for abnormalities. Seizures were controlled with the addition of Vimpat and Dilantin. The diagnosis of HHV6 encephalitis was made by HHV6 viremia (215,000 copies/mL on 18-Nov-2019) and positive lumbar puncture for HHV6 on 22-Nov-2019. Foscarnet was started on 20-Nov-2019. The new onset seizure activity was thought to be related to HHV6 encephalitis. The patient was transferred to the neuro ICU for close monitoring. The patient's tacrolimus level was 6.8 ng/mL on 20-Nov-2019, which was in therapeutic range.

No seizure activity was noted on 24-Nov-2019. Mental status and responsiveness to stimuli improved. The patient was transferred back to the BMT unit on 25-Nov-2019. On 30-Nov-2019, the patient became acutely tachycardic and was unable to respond to commands. Neurology was consulted and EEG did not show additional seizure activity. CT and MRI were negative for acute changes.

Jakafi was added on 24-Nov-2019 and the dose was maximized on 04-Dec-2019. The patient continued to have large volume stool output of greater than 2 liters per day. The patient's stool was noted to be bloody on 29-Nov-2019. Hemoglobin and hematocrit remaining stable until 01-Dec-2019. DIC screen indicated low

fibrinogen and increased D-Dimer although INR was within normal limits. Monitoring of complete blood counts, including a coagulation panel, was increased to every 6 hours. The patient required cryoprecipitate approximately every 2 days during the time frame of 01-Dec-2019 to 08-Dec-2019 and his fibrinogen eventually normalized. The patient required transfusions of RBC and platelets every 1-3 days. Due to major fluid losses, the patient was noted to have ongoing hypernatremia. The hypernatremia resolved with additional IV fluids.

The patient was started on Entyvio to replace tocilizumab on 19-Dec-2019 and another dose of Octreotide was given with some decrease in stool output by 27-Dec-2019. The patient continued to remain stable until 27-Dec-2019. On 27-Dec-2019, the nurse noted that the patient had exophthalmos that was more prominent in the right than left eye. A STAT head CT was ordered and was negative for a bleed. The patient and his family elected to go home at this point with home hospice. The patient was discharged home under the care of hospice on 28-Dec-2019.

The patient passed away on 30-Dec-2019. Primary cause of death was noted as acute GvHD and secondary cause was noted as viral infection. Autopsy was not performed.

Subject Identifier	GP3DUK-021
Age	58
Sex	Female
Baseline Weight (kg)	82.3
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	26 Feb 2020
Event	1. Relapse 2. PGF
Severity	1. Grade 5 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 24 Mar 2020 – 24 Oct 2020 2. 11 Mar 2020 – 25 Apr 2020
Outcome Of Event	1. Resolved by death 2. Persistent condition
Relationship To The Study Drug	1. No 2. Yes
Date Of Death (If Applicable)	24 Oct 2020

Narrative:
Patient GP3DUK-021 is a 58 year-old White female with Myelodysplastic Syndrome who received a Omidubicel transplant on 26-Feb-2020. Of note, the product TNC for the NF was below the release specifications of $\geq 4.0 \times 10^8$, with a final result of 3.9×10^8. Therefore, the product was infused under special FDA permission, in agreement to consider the product within specifications.

The patient was diagnosed with Myelodysplastic Syndrome on 15-May-2016. She underwent induction therapy with azacitidine every four weeks from May-2016 to 21-Jul-2017, and then every six weeks until 16-Dec-2019. The patient's past medical history included coronary artery disease (estimated EF 50%), depression, breast cancer (1996), hypertension, hypothyroidism, osteopenia, and recurrent urinary tract infections. Her surgical history included partial mastectomy/lumpectomy (1996), reduction mammaplasty (2002), and total abdominal hysterectomy and bilateral salpingo-oophorectomy (2001).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (17-Feb-2020 to 21-Feb-2020), fludarabine 60 mg/day (21-Feb-2020 to 24-Feb-2020), and thiotepa 280 mg/day (15-Feb-2020 to 16-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, acyclovir, and posaconazole. Neutrophil counts

recovered at 12 days post-transplantation (09-Mar-2020). The patient was discharged from the hospital on 31-Oct-2019.

A frozen research sample taken on 11-Mar-2020 (post-transplantation day +14) was sent for chimerism testing. Results revealed 82% donor cells which met the protocol definition of PGF (ANC > 500 for three consecutive measurements without donor chimerism > 90%). On 15-Mar-2020, the patient was found to have blasts in her peripheral blood. Given concern for high-risk of relapse, a BM biopsy was performed on 24-Mar-2020. The findings showed moderate to severe dysplasia in megakaryopoiesis, highly suggestive of a persistent myelodysplastic neoplasm. Relapse of primary disease was confirmed on 24-Mar-2020.

On 30-Mar-2020, mycophenolate mofetil and tacrolimus were stopped. Treatment with azacitidine 56 mg/m^2 intravenously for five doses was initiated on 06-Apr-2020 along with venetoclax 100 mg by mouth daily which was started on 07-Apr-2020. The PGF was noted as a persistent condition and the event was reported as resolved as of 25-Apr-2020.

In June 2020, the patient's performance status declined. She had marked exertional dyspnea. The patient remained transfusion independent at that time and was started on azacitidine at home.

The site personnel discovered that the patient had died on 24-Oct-2020 while doing an obituary search prompted by a missed study visit. The patient died at home and there were no medical records available for review. The site investigator deemed the primary cause of death to be relapse of disease.

Subject identifier	GP3DUP-001
Age	18
Sex	Male
Baseline weight (kg)	50.0
Race	Caucasian
Study therapy	Omidubicel
Date of study therapy administration	25 May 2018
Event	1. GvHD 2. Disease Relapse
Severity	1. Grade 2 2. Grade 3
Serious (yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 03 Aug 2018 – 15 Aug 2018 2. 13 Feb 2019 – 17 Jul 2019
Outcome of event	1. Resolved 2. Resolved
Relationship to the study drug	1. Yes 2. No
Date of death (if applicable)	03 Aug 2021

Narrative:
Participant GP3DUP-001 is an 18 year-old Caucasian male with Acute Lymphocytic Leukemia and therapy-induced Myelodysplastic Syndrome who received an omidubicel transplant on 25-May-2018.

The participant was diagnosed with Philadelphia chromosome positive Acute Lymphocytic Leukemia in January 2014. He was started on induction chemotherapy per AALL1131 on 10-Jan-2014. On Day 4 of induction therapy, cytogenetics and FISH results were positive for BCR-ABL1 fusion, so he was started on dasatinib and continued therapy per AALL0622, including consolidation and maintenance therapy. AALL 0622 consolidation #1 was initiated on 14-Feb-2014 and #2 on 07-Mar-2014, re-induction block #1 on 01-Apr-2014, re-induction block #2 on 28-Jul-2014, intensification block #2 on 08-Aug-2014, and maintenance on 24-Oct-2014. Cytogenetics and FISH on 26-Jan-2016 confirmed an abnormal karyotype and MLL rearrangement. The participant was then evaluated in February 2016 for potential transplant. A repeat bone

marrow performed during the pre-transplant work-up revealed resolution of the MLL rearrangement, so the participant was transferred back to his local oncologist for continued chemotherapy. The participant completed 12 cycles of maintenance therapy on 01-Nov-2016. A repeat bone marrow on 09-Nov-2016 showed no leukemia by morphology or flow cytometry, and FISH was negative for MLL and BCR-ABL1. However, PCR continued to show 0.257% BCR-ABL1 fusion, so the participant was continued on oral dasatinib as maintenance therapy until 02-May-2018.

The participant was diagnosed with therapy-induced Myelodysplastic Syndrome (MDS) on bone marrow evaluation on 07-Feb-2018. The bone marrow revealed increased myeloid blasts by morphology (approximately 5-6% of analyzed cells, no definitive evidence of B-lymphoblasts). Abnormal karyotype by cytogenetics, MLL translocation and Trisomy 8 by FISH, and BCR-ABL by PCR, sub-type RAEB-1 (Refractory Anemia with excess blasts) were also found. Therapy-induced Myelodysplastic Syndrome was therefore the indication for study enrollment. The participant's past medical history also included fungemia (March 2014), typhlitis (May 2015), necrotizing fasciitis (May 2015), pneumocystis jiroveci pneumonia with significantly reduced pulmonary function requiring intubation (December 2015), treatment related prolongation of QTc (March 2014), depression (2014, early in treatment), and fasciotomy (May 2015).

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of total body irradiation 1320 cGy (8 fractions of 165 cGy each; 21-May-2018 to 24-May-2018), fludarabine 40 mg/day (17-May-2018 to 19-May-2018), and cyclophosphamide 3100 mg/day (17-May-2018 and 18-May-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Other medications included acyclovir, albuterol, ciprofloxacin, cyproheptadine, dronabinol, filgrastim, home TPN, hydrocortisone, immunoglobulin, olanzapine, ondansetron, pantoprazole, pentamidine, tacrolimus, and voriconazole. Neutrophil counts recovered at 11 days post-transplantation (05-Jun-2018) and post-transplant chimerism was >98% donor. The participant was discharged from the hospital on 28-Jun-2018.

The participant's post-transplantation course was complicated by mild skin GvHD. The participant remained on TPN for nutritional support as he struggled with his appetite and maintaining weight. The participant underwent an upper endoscopy and flexible sigmoidoscopy on 02-Aug-2018. Surgical pathology reports documented evidence of mild chronic antral gastritis, acute esophagitis, and mildly increased epithelial apoptosis in the basal glands on biopsy of the sigmoid colon and rectum which were consistent with GvHD. Solumedrol was initiated at 2mg/kg/day on 02-Aug-2018, cyclosporine was changed to tacrolimus, and mycophenolate mofetil was discontinued. The participant was admitted to the hospital on 03-Aug-2018 for management of acute GvHD of the gut, persistent cough of unclear etiology, and weight loss.

On admission the participant had a progressively worsening dry cough without respiratory compromise. His chest x-ray was normal. He appeared to have upper airway irritation. The participant's GI symptoms improved, and methyl-prednisolone was slowly weaned. The participant's TPN was discontinued during admission as the participant's appetite and oral intake improved on appetite stimulants. Enteral prednisone was tried (40 mg PO twice daily) on 12-Aug-2018, but the participant developed abdominal pain. The participant's stools became formed and he even experienced some constipation as seen on abdominal x-ray on 13-Aug-2018. The constipation resolved with miralax. The participant was switched back to IV methyl-prednisolone (1.2 mg/kg/day) on 13-Aug-2018. At the time of discharge, the participant was having soft formed stools 1-2 times a day. The GvHD event was reported as resolved on 15-Aug-2018.

The participant was diagnosed with disease relapse on 13-Feb-2019. As part of routine workup, the participant underwent a bone marrow biopsy on 13-Feb-2019 which showed 2% abnormal blasts with a phenotype similar to his previous MDS blast population. Cytogenetics showed a single cell with the recurrent t(11;19) consistent with the participant's previously identified clone. The participant was confirmed to have relapsed disease on 22-Apr-2019 with 11% abnormal blasts in bone marrow aspirate exam. At the last study visit, the disease relapse event was still ongoing as the participant was receiving chemotherapy at his local hospital. The participant completed the study (month 15) as of 17-Jul-2019. Therefore, the disease relapse event is considered resolved by convention as of the last study visit date.

The participant later had worsening cytopenias. A bone marrow exam on 15-Sep-2020 revealed 20% MLL and 29% trisomy 8 by FISH (BCR-ABL negative) confirming relapse of disease. The MDS progressed into AML

after September 2020, date unknown. He developed multiple infections and became intolerant to further chemotherapy. The participant died of AML on 03-Aug-2021. An autopsy was not done.

Subject Identifier	GP3HFM-001
Age	50
Sex	Male
Baseline Weight (kg)	100.5
Race	Black – African American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	20 Feb 2020
Event	CMV Reactivation
Severity	Grade 2
Serious (Yes/no)	Yes
Start/stop date of Event	16 Mar 2020 – 09 Jun 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3HFM-001 is a 50 year-old Black, African American male with AML who received an Unmanipulated CBU transplant on 20-Feb-2020.

The patient was diagnosed with AML on 03-Aug-2012. Diagnostic molecular testing showed that 44% of nuclei had three copies of the AML1 probe region, possibly indicating the presence of a cell population with aneuploidy of chromosome 21 or less likely structural abnormalities involving the AML1 locus other than t(12;21). Induction therapy with cytarabine and idarubicin (7+3) was started on 03-Aug-2012. Four cycles of consolidation therapy with HiDAC were given from 08-Oct-2012 to 31-Dec-2012. The patient's disease relapsed in November 2019. He received reinduction therapy with fludarabine, cytarabine, G-CSF, and idarubicin on 13-Nov-2019 and HiDAC on 20-Dec-2019. The patient's past medical history included myocardial infarction, coronary artery disease, major depression, diabetes, pituitary microadenoma, hyperlipidemia, non-alcoholic steatohepatitis, male hypogonadism, and a left renal cell carcinoma. He had moderate pulmonary impairment at study screening. Surgical history included pituitary microadenoma removal (1998), laminectomy (1998), sigmoidectomy (2002), and a partial left nephrectomy (2017). The patient had reported allergies to ACE inhibitors.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of thiotepa 415 mg/day (13-Feb-2020 to 14-Feb-2020), fludarabine 99.5 mg/day (15-Feb-2020 to 17-Feb-2020), and busulfan 264.6 mg/day (15-Feb-2020 to 17-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included ciprofloxacin, acyclovir, voriconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 19 days post-transplantation (10-Mar-2020). The patient was discharged from the hospital on 11-Mar-2020. The post-transplant course was complicated by an episode of atrial fibrillation and bacteremia.

The patient was noted to have reactivated CMV during a regularly scheduled clinic visit on 16-Mar-2020. He was admitted for treatment with intravenous foscarnet. Foscarnet was given 16-Mar-2020 to 24-Mar-2020 and then switched to ganciclovir from 25-Mar-2020 to 29-Mar-2020. The patient was discharged home on valganciclovir on 30-Mar-2020. Valganciclovir was discontinued when the CMV viral load was negative. Letemovir was then started as prophylaxis. The CMV reactivation event was reported as resolved on 09-Jun-2020.

Subject identifier	GP3HSP-001
Age	13
Sex	Male

Baseline weight (kg)	62.3
Race	White – South or Central American
Study therapy	Omidubicel
Date of study therapy administration	17 Dec 2018
Event	Relapse
Severity	Grade 3
Serious (yes/no)	Yes
Start/stop date of Event	07 Aug 2019 – 02 Nov 2019
Outcome of event	Resolved
Relationship to the study drug	No
Date of death (if applicable)	27 Mar 2021

Narrative:
Participant GP3HSP-001 is a 13 year-old White, South or Central American male with Acute Myelogenous Leukemia who received an omidubicel transplant on 17-Dec-2018.

The participant was diagnosed with Acute Myelogenous Leukemia [FLT3 positive AML with maturation (M2), no favorable risk features] on 05-Jun-2018. He underwent two cycles of induction with etoposide, mitoxantrone, cytarabine, and intrathecal methotrexate from 06-Jun-2018 to 17-Jun-2018 and etoposide, cytarabine, daunorubicin, and intrathecal methotrexate from 30-Jul-2018 to 08-Aug-2018. He received consolidation therapy with mitoxantrone, cytarabine, and intrathecal methotrexate (06-Sep-2018 to 10-Sep-2018) and maintenance chemotherapy with azacitidine (22-Oct-2018 to 28-Oct-2018 and 19-Nov-2018 to 25-Nov-2018). The participant was in CR1 at study screening. The participant's past medical history included cardiac impairment. He had an ejection fraction of 50% at study screening.

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine 74 mg/day (12-Dec-2018 to 14-Dec-2018), thiotepa 260 mg/day (10-Dec-2018 to 11-Dec-2018), and busulfan 170-210 mg/day (12-Dec-2018 to 14-Dec-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Neutrophil counts recovered at 17 days post-transplantation (03-Jan-2019). The participant was discharged from the hospital on 18-Jan-2019.

The participant was admitted on 07-Aug-2019 for management of disease relapse. The participant presented to the emergency department with 24 hours of asthenia and hematomas. Blood tests showed hemoglobin 112g/L, platelets 8x10e9/L, and leukocytes 4.48x10e9/L (neutrophils 940, leukoblasts 580). The participant did not have hepatosplenomegaly or any other symptoms. The participant was transferred to another facility on 13-Aug-2019 to continue treatment with an anti-FLT3 trial drug. The goal was to get the participant into remission in order to perform another allogenic stem cell transplant.

The participant completed chemotherapy treatment without complications. On the 12-Sep-2019 a bone marrow aspiration was performed. The results showed that there were no blasts in the bone marrow, but bone marrow aspiration was not representative because the participant was in aplasia. The participant then had hematological recovery, and a new bone marrow aspiration performed on 02-October-2019 showed normal morphology. The participant was determined to be in remission on 02-Oct-2019 at which point the relapse event was considered resolved. On 09-Oct-2019, a bone marrow aspiration repeated at the study site was confirmed as negative.

The participant received a second allogenic stem cell transplant from an un-related donor (HLA compatibility 9/10) on 19-Nov-2019. The conditioning regimen was ATG, fludarabine, and melphalan. The infusion procedure was uneventful. Post-transplantation the participant developed cutaneous acute GvHD grade I that was controlled with steroids dose 0.5 mg/kg/day.

The participant's disease relapsed again on 11-Nov-2020. He was enrolled onto a phase I/II multi-center, dose-escalating study to evaluate quizartinib in combination with reinduction chemotherapy and as a single-agent maintenance therapy for participants with FLT3-ITD+ AML. He received another stem cell transplant on 12-Dec-2020. The participant died on 27-Mar-2021 due to pulmonary and renal failure, cardiac arrhythmia, and TMA. Secondary cause of death included disease relapse. An autopsy was not performed.

Subject Identifier	GP3IAE-001
Age	22
Sex	Female
Baseline Weight (kg)	48.7
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	17 Mar 2020
Event	1. Veno-occlusive Hepatic Disease 2. Bronchopneumonia 3. Fever 4. Septic Shock
Severity	1. Grade 4 2. Grade 4 3. Grade 2 4. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 23 Mar 2020 – 14 Apr 2020 2. 03 May 2020 – 16 Jul 2020 3. 20 Aug 2020 – 24 Aug 2020 4. 16 Nov 2020 – 05 Dec 2020
Outcome Of Event	1. Resolved with sequelae 2. Resolved 3. Resolved 4. Resolved by death
Relationship To The Study Drug	1. No 2. No 3. No 4. No
Date Of Death (If Applicable)	05 Dec 2020

Narrative:
Patient GP3IAE-001 is a 22 year-old White female with ALL who received an Unmanipulated CBU transplant on 17-Mar-2020.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor B-Cell ALL) on 09-Apr-2008. She underwent induction therapy with BFM95 protocol (Apr-2008 to 2010) and consolidation therapy with BFM REC 2002 protocol (Apr-2012 to Apr-2015). The patient also received 23 sessions of local radiotherapy for dermal infiltration in the left frontal region. Reinduction therapy included two cycles of blinatumomab and R-Hyper-CVAD (Jun-2019 to Sep-2019). Disease relapse was confirmed on 23-Jan-2020 and delayed transplantation. Additional reinduction therapy was then administered with inotuzumab (04-Feb-2020, 14-Feb-2020, and 21-Feb-2020). The patient had severe pulmonary impairment at study screening. Her past surgical history included prosthesis arthroplasty of the hip and femur (2014). She had reported allergies to penicillin, tramadol, and bromopride.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 200 cGy (09-Mar-2020 to 11-Mar-2020), thiotepa 225 mg (07-Mar-2020 to 08-Mar-2020), and fludarabine 60mg (12-Mar-2020 to 15-Mar-2020). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, trimethoprim-sulfamethoxazole, ganciclovir, pentamidine, and ciprofloxacin. Neutrophil counts recovered at 26 days post-transplantation (12-Apr-2020).

On 23-Mar-2020, the patient was receiving inpatient post-transplantation care when she developed painful hepatomegaly and massive ascites. She was noted to have a 10% increase in body weight. The patient was given diuretics and placed on hydration restriction. Labs revealed an elevation of liver enzymes by more than

6%, an increase in bilirubin, and a rapidly elevating creatinine. The patient was started on defibrotide. She became less responsive and required supplemental oxygen. The patient was moved to intensive care, where she remained hemodynamically stable. The patient's labs then showed improvements in levels of ammonia, CRP, and transaminases. An abdominal ultrasound on 31-Mar-2020 was suggestive of VOD. The patient was placed on continuous hemodialysis. As of 06-Apr-2020, the patient was stable, and her liver profile was improving. The patient remained stable but with ascites and was discharged from the hospital on 14-Apr-2020.

On 03-May-2020, the patient had severe respiratory failure and underwent orotracheal intubation for mechanical ventilation. A chest CT performed on 04-May-2020 revealed bilateral ground-glass opacities and diffuse alveolar condensations, particularly in the upper left and lower right lobes. The patient was already receiving acyclovir, meropenem, levofloxacin, and amphotericin B for a Grade 3 lung infection. COVID-19 test collected on 04-May-2020 was negative. The patient underwent a bronchoalveolar lavage on 07-May-2020 which returned positive for CMV. Peripheral blood sample was negative. Gancyclovir was initiated but then stopped on 11-May-2020 due to a lack of detection of CMV in the peripheral blood. Repeat scans of the chest, abdomen, and sinuses were performed on 14-May-2020 which showed improvements in the pulmonary condensation but significant liquid distension of the intestinal loops. The patient was extubated on 18-May-2020 but remained in the ICU.

On 01-Jun-2020, an infectious PET-CT scan was performed which continued to show improvement in the pulmonary condensation, without new focus. The meropenem was discontinued but amikacin and vancomycin were continued for 14 days of treatment. Prophylaxis was continued with pentamidine, micafungin, and valacyclovir.

The patient was intubated again on 02-Jun-2020 due to respiratory failure. A bronchoalveolar lavage on 03-Jun-2020 revealed the presence of CMV. All other cultures (respiratory panel, direct tuberculosis, strongyloidiasis, bacteria, and COVID) were negative. The patient was started on parenteral nutrition. Voriconazole was started on 04-Jun-2020. The patient was subsequently transferred out of the ICU and the bronchopneumonia event was considered resolved with no residual effect on 16-Jul-2020.

The patient was then admitted on 20-Aug-2020 with fever, hypotension, and a drop in her general condition. Lab results were negative for CMV, EBV, COVID-19, HHV6, adenovirus, and toxoplasmosis. Bone marrow showed a normal myelogram. Imaging of the chest, abdomen, and sinuses was normal. No definitive diagnosis was discovered, and the patient was discharged on 24-Aug-2020.

On 17-Nov-2020, the patient's mother informed the transplant center that her daughter had been admitted to an outside hospital on 16-Nov-2020 on suspicion of pneumonia. A tomography exam was performed but results were not available at the time of the call. The patient was started on antibiotic therapy with piperacillin-tazobactam on 16-Nov-2020.

The transplant center received a medical report from 18-Nov-2020 stating that the patient was admitted to the hospital with dehydration, hyporexia, and generalized asthenia – all Grade 4 and possibly related to the transplant procedure. On physical examination, the patient was depressed, hypoactive, and poorly communicative. She had a distended abdomen which was hypertympanic and painful to superficial palpation of the region. The patient's labs showed a drop in hemoglobin and hematocrit, worsening of the WBC count, progressive thrombocytopenia, increased renal markers, and coagulopathy. The patient underwent a CT scan of the abdomen that showed moderate distention of the colon with a predominance of the right hemicolon. The treating team considered the possibility of GvHD. A chest CT showed a major bilateral pleural effusion associated with small basal passive atelectasis on the right. A small amount of perihepatic fluid was noted. The patient received guided transfusion of blood products (filtered and phenotyped red cells and fresh frozen plasma) and erythropoietin. A *Clostridium* infection was suspected for which toxin and PCR tests were sent. Results were not provided at the time of the report.

According to a verbal update from the patient's mother on 03-Dec-2020, the patient remained hospitalized with septic shock, pneumonia, respiratory failure, and acute renal failure. The patient was on dialysis and mechanical ventilation. On 20-Nov-2020, piperacillin-tazobactam was suspended. Meropenem and vancomycin were started on 01-Dec-2020. A CMV test returned positive as did an indication of Grade 1

intestinal GvHD. The site continued to wait for medical records from the outside facility. The patient's mother informed the transplant center that a blood culture from 03-Dec-2020 was positive for *Pseudomonas aeruginosa* (grade 3 infection).

The patient's mother informed the transplant center that the patient died at dawn on 05-Dec-2020 from septic shock with *P. aeruginosa*. The site reported sepsis as primary cause of death. An autopsy was not done.

Subject Identifier	GP3IAE-002
Age	25
Sex	Female
Baseline Weight (kg)	64.0
Race	Black
Study Therapy	Omidubicel
Date Of Study Therapy Administration	27 Feb 2020
Event	1. Human Herpesvirus 6 Infection 2. VOD
Severity	1. Grade 3 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 26 Mar 2020 – 26 Apr 2020 2. 17 Apr 2020 – 26 Apr 2020
Outcome Of Event	1. Death 2. Death
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	26 Apr 2020

Narrative:
Patient GP3IAE-002 is a 25 year-old Black, Hispanic or Latino female with CML who received a Omidubicel transplant on 27-Feb-2020.

The patient was diagnosed with CML (chronic phase with no history of blast crisis) on 23-Oct-2017. She received induction therapy with hydroxyurea for one month. The disease was stable and not in hematologic remission pre-transplant. The patient's past medical history included hemorrhagic pancreatitis since 2018. She had severe pulmonary impairment at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 90 mg/day (22-Feb-2020 to 24-Feb-2020), thiotepa 335 mg/day (20-Feb-2020 to 21-Feb-2020), and busulfan 126-220 mg/day (21-Feb-2020 to 23-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, ciprofloxacin, micafungin, voriconazole, ganciclovir, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at eight days post-transplantation (06-Mar-2020). The patient was discharged from the hospital on 23-Mar-2020.

The patient was hospitalized for management of Human herpes virus 6 infection on 26-Mar-2020. On 28-Mar-2020 she had an episode of fever and dysuria. Cultures were collected and piperacillin/tazobactam was started. On 29-Mar-2020 she had a new episode of fever and increased CRP, without symptoms of infectious localization. Lung imaging on 02-Apr-2020 found signs of slight pulmonary congestion at the apexes and random diffuse micronodular miliary infiltrates in both lungs. The patient deteriorated and was intubated on 04-Apr-2020. Chest CT on 06-Apr-2020 found a miliary pattern highly suspicious of pulmonary toxoplasmosis. Three PCR tests for COVID-19 were negative. The patient was treated with clindamycin and trimethoprim/sulfamethoxazole for toxoplasmosis. She was discharged from the ICU on 16-Apr-2020. At that time, the patient's nurse reported that the patient was neurologically disabled and appeared confused.

The patient's liver transaminases were noted to be elevated on 02-Apr-2020 (AST 230 U/L, ALT 194 U/L) and 09-Apr-2020 (AST 159 U/L, ALT 109 U/L). She was admitted on 17-Apr-2020 with continued abnormal liver tests and Grade 3 liver failure. Imaging studies revealed hepatosplenomegaly and a patent portal vein with a caliber at the upper limit of normal. A paracentesis was performed on 19-Apr-2020 and 1560 mL of ascitic fluid was removed. Due to suspicion for very severe veno-occlusive liver disease, treatment with defibrotide was initiated on 20-Apr-2020. Continuous dialysis was started on 21-Apr-2020 to improve volume management. The following day, the patient's condition progressed to life-threatening and changed to Grade 4 acute liver failure with hepatic encephalopathy, progressive increase of ammonia in laboratory tests, drop in factor V, and deficiency of coagulation factors.

During a diagnostic transjugular intraheptic portosystemic shunt (TIPS) procedure on 23-Apr-2020, bleeding in the portal vein, right hepatic artery, and renal artery led to hemorrhagic shock. The bleeding sites were embolized and the patient received multiple transfusions during the procedure (nine red blood cell concentrates, four platelet apheresis, plasma, and fibrinogen). The result of a biopsy done on 23-Apr-2020 confirmed the diagnosis of VOD. Liver function tests continued to be elevated (AST 891 U/L, ALT 366 U/L, ALKP 96 U/L, total bilirubin 2.3 mg/dL). The patient was then continued under intensive care. She had significant hemodynamic instability, mixed acidosis, and severe coagulopathy with a need for transfusion. The patient's mechanical ventilation was also difficult to manage. The patient then had myocardial ischemia on 25-Apr-2020. The patient's condition continued to worsen and evolved to multi-organ dysfunction which resulted in death on 26-Apr-2020. The primary cause of death was noted as organ failure, VOD. Autopsy was not done.

Deviations with potential medical significance: PCP prophylaxis was not given after neutrophil engraftment on 06-Mar-2020.

Subject Identifier	GP3KMC-001
Age	18
Sex	Male
Baseline Weight (kg)	72.5
Race	Caucasian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	18 Apr 2018
Event	1. GI Disorders: Nausea/Vomiting Related to Chemo 2. Meningismus 3. PGF 4. Lower GI GvHD - stage 4 5. Acute Respiratory Failure
Severity	1. Grade 3 2. Grade 2 3. Grade 3 4. Grade 5 5. Grade 4
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 13 Mar 2018 – 15 Mar 2018 2. 23 Mar 2018 – 25 Mar 2018 3. 31 May 2018 – 02 Jun 2018 4. 04 May 2018 – 15 Jun 2018 5. 12 Jun 2018 – 15 Jun 2018
Outcome Of Event	1. Resolved 2. Resolved

	3. Resolved 4. Death 5. Death
Relationship To The Study Drug	1. NA: Pre-Transplant Event 2. NA: Pre-Transplant Event 3. Yes 4. Yes 5. No
Date Of Death (If Applicable)	15 Jun 2018

Narrative:
Patient GP3KMC-001 is an 18 year-old Caucasian male with ALL who received an Unmanipulated CBU transplant on 18-Apr-2018.

The patient was diagnosed with ALL, subtype T-ALL (with NRAS, +Notch1, +Kit, +U2AF1 mutations) on 23-Jan-2018. He received one cycle of pediatric inspired induction chemotherapy starting on 24-Jan-2018. This included vincristine (days 1, 8, 15, 22), daunorubicin (days 1, 8, 15, 22), prednisone (days 1-28), pegasparagase (day 4), intrathecal (IT) methotrexate (days 1 and 29, plus days 15 and 22 if CSF positive), and IT cytarabine (day 8). He received one cycle of pediatric inspired consolidation therapy starting on 01-Mar-2018. This included mercaptopurine (days 1-14, 29-42), cyclophosphamide (days 1, 29), cytarabine (days 1-4, 8-11, 29-32, 36-39), vincristine (days 15, 22, 43, 50), pegaspargase (day 15, 43), and methotrexate IT (days 1, 8, 15, 22). The patient's past medical history included systemic inflammatory response syndrome, recent tachycardia, sinus bradycardia and PVCs on past ECG, acute DVT of the brachial vein, prior methotrexate-induced meningitis, sensitivity to phenothiazine (drug-induced headache), and moderate protein-calorie malnutrition. He had moderate hepatic impairment (ALT 171 U/L on 19-Mar-2018, 127 U/L on 20-Mar-2018, and 118 U/L 22-Mar-2018) at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/dose (nine doses from 09-Apr-2018 to 13-Apr-2018), fludarabine 57.25 mg/day (13-Apr-2018 to 16-Apr-2018), and thiotepa 316.50 mg/day (07-Apr-2018 to 08-Apr-2018). GvHD prophylaxis with cyclosporine and mycophenolate mofetil was started on 15-Apr-2018. Infection prophylaxis included fluconazole, levofloxacin, pentamidine, and trimethoprim-sulfamethoxazole.

Post-transplantation the patient had a lower respiratory rhinovirus/enterocolitis infection (22-Apr-2018) that involved fever and enterocolitis. The patient was treated with micafungin, vancomycin, and meropenem. The patient's hospital course was further complicated by neutropenic fever, multifocal pneumonia, GvHD involving his GI tract, HHV6 viremia, BK infection, coagulase-negative staph line infection, partial small bowel obstruction with suspicion of typhilitis, and persistent pancytopenia.

After receiving the UCB transplant on 18-Apr-2018 the patient's ANC was not showing any signs of rebounding. On 16-May-2018, the patient's physicians decided to double the dose of daily G-CSF from 300 mcg to 600 mcg. Nearing Day +42 (30-May-2018) the patient was still not showing signs of neutrophil engraftment (ANC 0.3 x 109/L) and the patient was declared to have PGF on Day +43 post-transplantation (31-May-2018). The physicians wanted to give the patient extra time to see if he would recover. His ANC began to recover on Day +45 (02-Jun-2018) with an ANC of 0.8 x 109/L. The PGF event was therefore considered resolved on 02-Jun-2018. The patient's ANC continued to steadily climb until Day +50 (07-Jun-2018) when the ANC briefly dropped for two consecutive days before finally recovering on Day+ 52 (09-Jun-2018).

Post-transplantation, the patient had persistent diarrhea which continued after a CT on 27-Apr-2018 which was negative for colitis. *C. difficile* tests were negative, as were tests for rotavirus, giardia, cryptovirus and adenovirus. The patient was continued on diphenozylate/atropine (Lomotil) as scheduled and opium tincture was added. Endoscopy on 04-May-2018 showed both upper and lower GvHD. The patient was started on steroids on 06-May-2018. With worsening diarrhea, the steroid dose was maintained at 0.8 mg/kg. EGD and flexible sigmoidoscopy were performed on 04-Jun-2018. Results showed gastric mucosa Grade I GvHD and colonic mucosa Grade II GvHD. CMV and HSV-1 were negative. The patient was started on extracorporeal photopheresis (ECP) three times a week on 07-Jun-2018. Ruxolitinib (Jakafi) was started on 8-Jun-2018.

The patient also continued to have significant pain with urination due to BK cystitis. Continuous bladder irrigation was done from 8-Jun-2018 to 11-Jun-2018 with some relief. Repeat CT abdomen on 11-Jun-2018 showed progressive colonic dilation and enteritis, and progression of small bowel dilation. Oral medications were held over the concern for small bowel obstruction and decompensation. The patient was ordered to have nothing by mouth, GI consult was obtained, and a nasogastric tube was used for decompression. An abdominal CT scan performed on 14-Jun-2018 showed pneumatosis. Surgery consult was obtained, and the team met with the family. The decision was made not to proceed with surgery given diffuse GvHD and unlikely helpful surgical intervention.

A code/rapid response was called on 12-Jun-2018 because of an early warning score of 8. At the time the patient's respirations were labored with a new oxygen requirement of 2 L oxygen. The patient was transferred to the ICU for apparent shortness of breath, hypoxemia, tachypnea, and elevated early warning score. In the ICU, he received platelets and PRBCs. Workup was initiated for sepsis.

Hemodialysis was initiated on 14-Jun-2018 and the patient's TPN was continued. Treatment for GvHD was continued including methylprednisolone and tocilizumab as per BMT recommendation. Ultimately the decision was made to transition the patient to comfort measures overnight on 14-Jun-2018. The patient was transitioned from fentanyl to hydromorphone and he appeared more comfortable. He was pronounced dead on 15-Jun-2018. Primary cause of death was noted as acute GvHD. Autopsy was not performed.

Deviations with potential medical significance: Gamida Cell granted a deviation to the protocol-specified fludarabine dosing via email communication on 28-Mar-2018. The PI felt that it was in the best interest of the patient, who had previously received intrathecal methotrexate and had a history of methotrexate-induced meningeal inflammation, to receive a 20% dose reduction.

Subject Identifier	GP3KMC-002
Age	46
Sex	Female
Baseline Weight (kg)	82.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	08 May 2019
Event	Acute Hypoxemic Respiratory Failure
Severity	Grade 5
Serious (Yes/no)	Yes
Start/stop date of Event	16 May 2019 – 12 Jun 2019
Outcome Of Event	Death
Relationship To The Study Drug	No
Date Of Death (If Applicable)	12 Jun 2019

Narrative:
Patient GP3KMC-002 is a 46 year-old White female with AML who received an Unmanipulated CBU transplant on 08-May-2019.

The patient was diagnosed with AML (Acute monoblastic / acute monocytic leukemia - M5) on 04-Feb-2019. Her treatment included induction 7+3 with cytarabine and daunorubicin (07-Feb-2019). The patient's past medical history included traumatic brain injury, post-traumatic stress disorder, anxiety, depression, uterine and bladder prolapse, migraines, chronic neck pain, and sleep disturbance. Surgical history included three cesarean sections, cholecystectomy (2016), shoulder surgery, and wisdom teeth extraction. The patient reported allergies to alprazolam and ondansetron.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 79 mg/day (03-May-2019 to 05-May-2019), thiotepa 294 mg/day (01-May-2019 to 02-May-2019), and busulfan 275 mg/day (03-May-2019 to 05-May-2019). GvHD prophylaxis included

mycophenolate mofetil and cyclosporine. Neutrophil counts recovered at 13 days post-transplantation (21-May-2019).

The patient received the study transplant on 08-May-2019 without any complications. During the post-transplant period, she started experiencing a productive cough, wheezing, dyspnea, and hypoxia which slowly worsened. Respiratory viral panel done on 11-May-2019 (nasal wash) was positive for metapneumovirus and she was started on broad-spectrum antibiotics. The patient had a CT done on 12-May-2019 which showed moderate interstitial type pneumonia in the LUL. No alveolar consolidation or pleural effusion was noted. She had neutropenic fevers on 13-May-2019. Due to worsening symptoms and development of an oxygen requirement (2 L), a bronchoscopy was performed on 16-May-2019. Shortly after the procedure, the patient was in acute hypoxic respiratory failure, requiring 15 L of oxygen per nasal cannula. The patient's oxygen saturation was in the mid-80s. The patient was transferred to the ICU on 16-May-2019 for management of acute hypoxic respiratory failure secondary to viral infection.

A chest x-ray taken on 16-May-2019 showed diffuse pneumonia. Respiratory viral panel performed on a bronchoalveolar lavage specimen was positive for human metapneumovirus on 16-May-2019. The patient needed high-flow oxygen and was at risk for intubation, requiring ICU level supervision. She was treated with oral ribavirin from 17-May-2019 to 21-May-2019. As of 20-May-2019, the patient still required high-flow oxygen and remained at high-risk of life-threatening deterioration. She remained in the ICU for continuous monitoring of acute hypoxic respiratory failure and was continued on antibiotics (meropenem, vancomycin, and cresemba).

Human herpes virus 6 (HHV-6) was detected in the patient's blood on 29-May-2019 with 91,400 copies/mL. The patient's antibiotic course was completed on 29-May-2019. Foscarnet was administered as treatment for the HHV6 viremia from 30-May-2019 to 12-Jun-2019. The patient was still positive for human metapneumovirus as of 02-Jun-2019. Another chest CT taken on 02-Jun-2019 showed marked progression in bilateral interstitial ground-glass and alveolar infiltrates most compatible with atypical pneumonia. The patient was restarted on meropenem and vancomycin on 03-Jun-2019 and was continued on cresemba.

Per the patient's wishes, she was transitioned to comfort measures and decided to be DNAR-CMO (Do Not Attempt Resuscitation-Comfort Medicines Only). All non-comfort medications and orders were discontinued. The patient passed away on 12-Jun-2019. Primary cause of death was noted as acute hypoxic respiratory failure, with secondary cause of death noted as viral infection. Autopsy was not done.

Deviations with potential medical significance: G-CSF therapy was stopped on day 1 of ANC>1000, and not the second consecutive day.

Subject Identifier	GP3KMC-003
Age	36
Sex	Male
Baseline Weight (kg)	104.6
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	23 Jul 2019
Event	1. HHV6 Reactivation 2. Skin Infection 3. Fatigue 4. Graft-Versus-Host Disease
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 5
Serious (Yes/no)	1. Yes 2. Yes

	3. Yes 4. Yes
Start/stop date of Event	1. 10 Sep 2019 – 15 Sep 2019 2. 07 Oct 2019 – 16 Oct 2019 3. 21 Oct 2019 – 21 Dec 2019 4. 07 Aug 2019 – 21 Dec 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Death 4. Death
Relationship To The Study Drug	1. No 2. No 3. No 4. Yes
Date Of Death (If Applicable)	21 Dec 2019

Narrative:
Patient GP3KMC-003 is a 36-year-old White male with AML who received an Unmanipulated CBU transplant on 23-Jul-2019.

The patient was diagnosed with AML on 25-Apr-2019. He underwent treatment with induction 7+3 chemotherapy starting on 26-Apr-2019 and consolidation idarubicin cytarabine (IDAC) chemotherapy starting on 07-Jun-2019. The patient's past medical history included obesity, hypertension, heart palpitations, DVT, and febrile non-hemolytic transfusion reaction. He had mild hepatic and moderate pulmonary impairment at study screening. Surgical history included cholecystectomy (28-Oct-2016) and tonsillectomy (2015). He had reported allergies to cefepime, Meropenem, and Zosyn.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 113 mg/day (18-Jul-2019 to 20-Jul-2019), thiotepa 480 mg/day (16-Jul-2019 to 17-Jul-2019), and busulfan 265 mg/day (18-Jul-2019 to 20-Jul-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, fluconazole, vancomycin, pentamidine, and Posaconazole. Neutrophil counts recovered at 24 days post-transplantation (16-Aug-2019).

Post-transplantation the patient experienced large amounts of diarrhea, abdominal cramping, and occasional nausea without vomiting. On 06-Aug-2019, GvHD was suspected and daily steroids were started at 1.6mg/kg. On 06-Aug-2019, stool studies were negative for Clostridium difficile, Cryptosporidium, Giardia, Norovirus, and Rotavirus. The patient was started on scheduled Lomotil with Imodium as needed.

A flexible sigmoidoscopy was performed on 07-Aug-2019 to evaluate for GvHD. Pathology results confirmed Grade 1 colon GvHD on 07-Aug-2019. Cyclosporine level on 10-Aug-2019 was 228 ng/ml, which was within therapeutic range. On 12-Aug-2019, daily stool output was >1500 ml. The patient received Mesenchymal Stem Cells for GI GvHD on 12-Aug-2019 and again on 19-Aug-2019. Beclomethasone and Entocort were also started. Cellcept was held for concern that the drug was contributing to the diarrhea. Jakafi was then started on 24-Aug-2019 for persistent GvHD. The patient was able to be discharged on 04-Sep-2019.

The patient then required re-admissions for issues including Human herpesvirus 6 infection (10-Sep-2019 to 15-Sep-2019), skin infection (07-Oct-2019 to 16-Oct-2019), fatigue (21-Oct-2019 to 14-Dec-2019), and GvHD. The patient began experiencing bloody stools. He underwent upper and lower gastrointestinal scopes on 22-Oct-2019. Results reported several non-bleeding erosions in the gastric antrum area, with normal mucosa of the esophagus and duodenum. No focal sites of bleeding were identified. The patient was then found to be Clostridium difficile positive on 02-Nov-2019. He received C. difficile treatment until 12-Nov-2019. The patient then trialed a Prednisone taper of 15 mg every other day alternating with 50mg every other day. This taper was stopped due to hyperbilirubinemia (Total Bilirubin 6.1 mg/dl), anorexia, and concern for chronic GvHD. Prednisone dose was then increased on 21-Nov-2019 to 1 mg/kg. Total bilirubin decreased to 2.9 mg/dl after the increase in steroids. Chronic GvHD was diagnosed on 22-Nov-2019.

The patient continued to decline clinically and enrolled in hospice on 14-Dec-2019. The patient passed away on 21-Dec-2019. The primary cause of death was noted as chronic GvHD.

Subject Identifier	GP3KMC-004
Age	33
Sex	Female
Baseline Weight (kg)	50.2
Race	Black – African American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	23 Oct 2019
Event	Acute Graft-versu- Host Disease
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	16 Dec 2019 – 22 Jan 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	Yes
Date Of Death (If Applicable)	

Narrative:
Patient GP3KMC-004 is a 33 year-old Black, African American female with ALL who received a Omidubicel transplant on 23-Oct-2019.
Note: The transplant occurred more than 90 days after study randomization.

The patient was diagnosed with ALL (BCR/ABL+ ALL) on 31-Jan-2019. She received induction therapy according to protocol CALB10403 from 03-Feb-2019 to 07-Mar-2019 and protocol AALL1122 from 11-Mar-2019 to 17-May-2019. Two cycles of consolidation therapy per AALL1122 were given from 20-May-2019 to 04-Jul-2019. The patient had mild hepatic impairment (AST = 78 U/L) and moderate pulmonary dysfunction (cDLCO 79%) at study screening. She had no reported drug allergies at screening.

The patient was first randomized to the Omidubicel study arm on 10-Jul-2019. On 15-Jul-2019, the patient received a round of chemotherapy per KMC01's standard of care. On 16-Jul-2019, bronchoscopy results suggested that the patient had an infection. She was placed on a 21-day treatment course. During the infection treatment course, the patient received another round of consolidation because of the delay. Gamida Cell was notified about the infection on 16-Jul-2020 and decided to continue Omidubicel production as planned. However, production was halted due to the patient's insurance coverage and concern that the patient would develop antibodies to the cord during consolidation. On 28-Aug-2019, the patient had a new biopsy and MRD was detected. On 03-Sep-2019, the patient was started on a 21-day cycle of blinatumomab for treatment of the MRD. Omidubicel production was restarted on 13-Sep-2019. On 24-Sep-2019, the patient presented to the clinic with acute sinus symptoms. The clinic team decided to delay transplant by two weeks after ENT consultation, thereby pushing the patient out of the 90-day study randomization window. The patient finally began study transplant conditioning on 14-Oct-2019.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (14-Oct-2019 to 18-Oct-2019), thiotepa 257.5 mg/day (12-Oct-2019 to 13-Oct-2019), and fludarabine 48.25 mg/day (18-Oct-2019 to 21-Oct-2019). Mycophenolate mofetil and cyclosporine were given as GvHD prophylaxis. Neutrophil counts recovered at nine days post-transplantation (01-Nov-2019). The patient was discharged from the hospital on 22-Nov-2019.

On 16-Dec-2019, the patient was seen for routine follow-up in clinic. The patient reported abdominal cramping, stomach gurgling, minimal stool output, anorexia, and nausea. She denied vomiting. She had a 6.8 kg weight loss since the previous assessment. The patient also reported dry mouth and eyes. The patient was noted to have a non-pruritic maculopapular rash on the face and neck. She was on a prednisone taper at the time. Following the exam, the patient was admitted for failure to thrive, progressive weight loss, and acute GvHD of the skin and GI system. Management of the GvHD included switching medications to intravenous

(IV) as well as replacing oral intake with TPN due to poor GI function, difficulty swallowing, and malnutrition. Methylprednisolone was given twice a day.

On 17-Dec-2019, the patient underwent a flexible sigmoidoscopy which showed sigmoiditis and proctitis. A biopsy obtained during the procedure was suggestive of GvHD. CMV stain was negative. During the admission, the patient was able to gain 10 kgs. On 23-Dec-2019, a steroid taper was started, and solumedrol IV was changed to oral prednisone. As the patient continued to improve, all medications were switched back to oral formulation. The patient was deemed suitable for home management and was discharged on 27-Dec-2019.

On 22-Jan-2020, the patient was seen for a regularly scheduled clinic visit. The provider confirmed that the GvHD was no longer clinically active. The acute GvHD event was deemed to be resolved with no residual effects.

Subject Identifier	GP3LAF-001
Age	21
Sex	Male
Baseline Weight (kg)	76.0
Race	Caucasian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	27 Feb 2017
Event	1. Relapse Acute Leukemia 2. ALL relapse in nervous system 3. Suicide attempt
Severity	1. Grade 3 2. Grade 4 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 11 Jan 2017 – 7 Feb 2017 2. 24 Jul 2017 – 06 Sep 2017 3. 06 Sep 2017 - 06 Sep 2017
Outcome Of Event	1. Resolved 2. Death 3. Death
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	06 Sep 2017

Narrative:
Patient GP3LAF-001 is a 21 year-old Caucasian male with ALL who was randomized to the study trial on 12-Jan-2017, was diagnosed with relapsed ALL (isolated CNS relapse) on 11-Jan-2017, and received a Omidubicel transplant on 27-Feb-2017.

The patient was diagnosed with ALL (Precursor T-cell) on 04-Mar-2016. He was treated with induction PETHEMA LLA-RI-2008 starting on 10-Mar-2016 and one course of consolidation therapy (03-May-2016 to 29-Jun-2016). His first relapse (isolated CNS relapse) was treated with FLAG-IDA (22-Sep-2016) and intrathecal treatment. Consolidation therapy then started on 12-Dec-2016 with remission achieved on 20-Dec-2016. The patient was diagnosed with isolated CNS relapse on 11-Jan-2017 during a routine lumbar puncture (LP) for intrathecal prophylaxis prior to the study product infusion. The patient had completed screening tests/procedures at the transplant center at that point, and the local oncologist did not inform the transplant center of the results of the LP before the date of randomization (12-Jan-2017). The patient then received intrathecal therapy weekly until two consecutive negative lumbar punctures. The cerebrospinal fluid sample

taken on 06-Feb-2017 by his local oncologist was reported negative for blast cells (immunophenotyping performed and was negative). His past medical history included left facial paralysis (suspicion of zoster infection, resolved with acyclovir and steroids) and moderate pulmonary function.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 100 mg/day (22-Feb-2017 to 24-Feb-2017), thiotepa 400 mg/day (20-Feb-2017 to 21-Feb-2017), and busulfan 260 mg/day (22-Feb-2017 to 24-Feb-2017). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included fluconazole, acyclovir, ciprofloxacin, posaconazole, and topical mupirocin. Neutrophil counts recovered at 14 days post-transplantation (13-Mar-2017). The patient was discharged from the hospital on 18-Mar-2017.

The patient presented with diplopia and was admitted for diagnostic studies on 24-Jul-2017. Lumbar puncture was done and the patient was diagnosed with ALL relapse in the nervous system on 24-Jul-2017. The patient was referred to a hospital near his home to continue symptomatic care on 27-Jul-2017. He received palliative radiotherapy in a hospital near his home through 21-Aug-2017, the last contact with the clinical center. The patient also had persistent neurological symptoms (ie dysphagia, cognitive disturbance) requiring hospitalization in a hospital near his home. On 15-Sep-2017, the site staff became aware that the patient had died on 06-Sep-2017 in the emergency room of the hospital near his home due to a suicide attempt at home. Per the clinical record, the patient had developed depression after ALL progression. Autopsy was not performed.

Subject Identifier	GP3LAF-002
Age	43
Sex	Female
Baseline Weight (kg)	78.0
Race	White – Caucasian
Study Therapy	Not received
Date Of Study Therapy Administration	N/A
Event	1. Relapse of Acute Leukemia 2. Sepsis
Severity	1. Grade 5 2. Grade 4
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 16 Jan 2017 – 24 May 2017 2. 15 Feb 2017 – 16 Mar 2017
Outcome Of Event	1. Death 2. Resolved
Relationship To The Study Drug	1. NA: Pre-transplant event 2. NA: Pre-transplant event
Date Of Death (If Applicable)	24 May 2017

Narrative:
Patient GP3LAF-002 is a 43 year-old White female with AML who consented to participate in the Omidubicel GP3 study on 21-Dec-2016. The patient did not receive the study transplant.

The patient was diagnosed with AML (NPM1+ FLT3+) on 05-Sep-2016. She underwent treatment with one cycle of induction therapy with 7+3 (cytarabine and daunorubicin) on 06-Sep-2016 and one cycle of consolidation therapy 7+3 (cytarabine and daunorubicin) on 01-Nov-2016. The patient's past medical history included hypothyroidism following a thyroidectomy due to Graves-Basedow disease. She had severe pulmonary impairment and mild hepatic impairment at study screening. The patient had no reported drug allergies at screening.

The patient was admitted for transplant on 16-Jan-2017 and blasts cells were observed in a routine lab draw of peripheral blood before starting the conditioning regimen. Hematologic relapse was confirmed with a BM examination. The patient was included in a clinical trial and assigned to receive fludarabine, cytarabine, filgrastim, and idarubicin (FLAG-IDA). The patient received the first dose on 20-Jan-2017. A repeat BM exam performed on 15-Mar-2017 revealed 98% blasts. A second cycle of FLAG-IDA was started on 21-Mar-2017.

During hospitalization for FLAG-IDA treatment, the patient developed a fever and blood stream infection (*Enterobacter cloacae*). The source of the infection was her catheter, and it was removed on 15-Feb-2017. The patient was started on intravenous (IV) antibiotics. The patient had still not recovered from chemotherapy at that time (ANC 0.00 mil/mm3 on 15-Feb-2017). After catheter removal, the *Enterobacter* infection persisted. Finally the patient improved with IV antibiotics, but she remained refractory to chemotherapy for the AML.

The patient's disease was deemed refractory to salvage treatment with FLAG-IDA. She was transferred to a hospital near her home for palliative care and died on 24-May-2017. The primary cause of death was noted as AML progression.

Deviations with potential medical significance: During screening, BM aspirate cytogenetics were not performed because the marrow showed no disease. The standard of care of the site was to freeze the sample because the result was going to be negative.

Subject Identifier	GP3LAF-005
Age	20
Sex	Male
Baseline Weight (kg)	75.0
Race	Caucasian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	11 May 2017
Event	1. Diarrhea 2. Hemorrhagic Cystitis 3. UTI 4. GvHD
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 11 Jun 2017 – 15 Jun 2017 2. 02 Jul 2017 – 07 Jul 2017 3. 15 Jul 2017 – 21 Jul 2017 4. 15 Aug 2017 – 23 Sep 2017
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Death
Relationship To The Study Drug	1. No 2. No 3. No 4. Yes
Date Of Death (If Applicable)	23 Sep 2017
Narrative:	

Patient GP3LAF-005 is a 20 year-old Caucasian male with AML who received an Unmanipulated CBU transplant on 11-May-2017.

The patient was diagnosed with AML without maturation (M1) on 18-Nov-2016. He was treated with induction idarubicin + cytarabine 3+7 (23-29-Nov-2016), consolidation #1 3+7 (17-23-Jan-2017), and consolidation #2 HiDAC (7, 9 and 11-Mar-2017). The patient had no other reported medical history.

Prior to UCB transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 100 mg (06-May-2017 to 08-May-2017), thiotepa 400 mg (04-May-2017 to 05-May-2017), and busulfan 260 mg (06-May-2017 to 08-May-2017). GvHD prophylaxis initially included mycophenolate mofetil and cyclosporine. Cyclosporine was stopped due to suspicion of thrombotic microangiopathy (TMA) and replaced with sirolimus. Other medications included amiodarone, Bactrim, lorazepam, nifedipine retard, insulin lispro, omeprazole, and magnesium. Neutrophil counts recovered at 21 days post-transplantation (01-Jun-2017). The patient was discharged from the hospital on 06-Jun-2017.

Post-transplantation the patient was hospitalized for diarrhea (11-Jun-2017 to 15-Jun-2017), hemorrhagic cystitis (02-Jul-2017 to 07-Jul-2017), and a UTI (15-Jul-2017 to 21-Jul-2017). The patient was then admitted to the hospital on 15-Aug-2017 for diarrhea. The patient was found to be positive for Clostridium difficile. He was treated with oral vancomycin and IV metronidazole. A colonoscopy performed on 23-Aug-2017 showed proctocolitis. On 23-Aug-2017, the patient was started on methylprednisolone at 2 mg/kg, but the patient's condition did not improve. CMV viral load was not detected as of 25-Aug-2017. On 28-Aug-2017, despite appropriate antibiotic treatment, the patient continued to have diarrhea accompanied with persistent abdominal pain. On 29-Aug-2017, extracorporeal photopheresis was started but did not result in improvement. On 31-Aug-2017, biopsy suggested the presence of graft vs host disease. GvHD worsened to Grade 4 (GvHD classification) on 05-Sep-2017, and the patient was started on infliximab. As of 18-Sep-2017, the GvHD had not responded to infliximab. The patient's condition worsened (Grade 4, life-threatening) and he developed paralytic ileus and severe abdominal pain, with persistent intestinal hemorrhage. The GvHD did not respond to infliximab or high-dose steroids. The patient's condition worsened and death occurred on 23-Sep-2017. Primary cause of death was noted as acute GvHD. Secondary cause of death was noted as organ failure, pulmonary. Autopsy was not performed.

Subject Identifier	GP3LAF-006
Age	27
Sex	Female
Baseline Weight (kg)	59.0
Race	Not reported
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	01 Aug 2017
Event	1. Anorectal Infection 2. Abdominal Pain 3. Anorectal Infection 4. GvHD 5. Anorectal Infection 6. Sepsis 7. Anorectal Infection
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3 5. Grade 3 6. Grade 4 7. Grade 3
Serious (Yes/no)	1. Yes 2. Yes

	3. Yes 4. Yes 5. Yes 6. Yes 7. Yes
Start/stop date of Event	1. 28 Aug 2017 – 05 Sep 2017 2. 27 Sep 2017 – 04 Oct 2017 3. 16 Oct 2017 – 06 Nov 2017 4. 21 Nov 2017 – 06 Mar 2018 5. 01 Jan 2018 – 15 Jan 2018 6. 31 Jan 2018 – 06 Mar 2018 7. 11 Mar 2018 – 18 Apr 2018
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Resolved 6. Resolved 7. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. Yes 5. No 6. No 7. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LAF-006 is a 27 year-old female with AML who received an Unmanipulated CBU transplant on 01-Aug-2017.

The patient was diagnosed with minimally differentiated AML (M0) on 13-Oct-2014. She was treated first line with daunorubicin plus cytarabine in 2014 and then maintenance with mercaptopurine and cytarabine. She then received second line therapy with FLAG-Ida (21-Mar-2017). Other medical history included moderate pulmonary function with DLCO and/or FEV1 of 66-80%. Surgical history included two cesarean sections and tubal ligation. She had positive CMV antibodies.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 80 mg/day (27-Jul-2017 to 29-Jul-2017), thiotepa 280 mg/day (25-Jul-2017 to 26-Jul-2017), and busulfan 180 mg/day (27-Jul-May-2017 to 29-Jul-2017). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Cyclosporine was withdrawn due to suspicion of microangiopathy and the patient was started on sirolimus. Other medications included ursodeoxycholic acid, valcyte, septrin forte, acfol, prednisone, magnesium, monosodium phosphate, posaconazole, parafine, insulin lantus, insulin humalog, potassium, and levofloxacine. Neutrophil counts recovered at 16 days post-transplantation (17-Aug-2017). The patient was discharged from the hospital on 05-Sep-2017.

Post-transplantation the patient was hospitalized for anorectal infection (26-Aug-2017), abdominal pain with constipation (27-Sep-2017), and again with anorectal infection (16-Oct-2017). The patient was then admitted to the hospital on 21-Nov-2017 with lower gastrointestinal hemorrhage requiring observation. A colonoscopy and biopsy were performed on 23-Nov-2017 which showed graft-versu- host disease. The patient's steroid dose was increased, and she was discharged on 28-Nov-2017. On 29-Nov-2017, the patient was readmitted to the hospital due to a new episode of lower gastrointestinal hemorrhage. She was under close observation and further treatment for GvHD was not immediately initiated. The patient was included in another clinical trial CINC424C2301 (after agreement of sponsor) for acute GvHD and was assigned to photopheresis (control arm). She started the first treatment on 05-Dec-2017. She did not have repeated hemorrhage and was discharged on 05-Dec-2017.

The patient was then re-hospitalized twice for lower gastrointestinal hemorrhage (09-Dec-2017 to 11-Dec-2017 and 14-Dec-2017 to 21-Dec-2017). A colonoscopy performed on 20-Dec-2017 showed superficial ulcers. Colonic biopsy confirmed graft vs host disease. In the colonic biopsy, cytomegalovirus was detected. The last episode of GI hemorrhage occurred on 25-Dec-2017. The patient continued treatment with steroids and photopheresis. A new episode of gastrointestinal hemorrhage then occurred on the 28-Jan-2018 when the patient was admitted for observation and transfusion support. She was discharged on 30-Jan-2018.

The patient was readmitted on 31-Jan-2018 to intensive care due to sepsis (fever, hypotension, and oliguria) and a small gastrointestinal hemorrhage. Noradrenalin was started. There was no clear source of the fever on admission. The patient showed improvement and noradrenalin was stopped on 03-Feb-2018. She was then transferred out of the ICU. The source of the infection was attributed to pseudomonas aeruginosa from perianal source. The patient's perianal infection was treated with IV antibiotics. During her hospital stay, the patient required surgery for cleaning and debridement of the perianal area three times (02-Feb-2018, 16-Feb-2018, and 28-Feb-2018). During this hospitalization and afterwards she did not have repeat hemorrhage. The patient improved clinically and was discharged on the 06-Mar-2018 at which point the sepsis and GvHD related events were considered resolved.

Subject Identifier	GP3LAF-007
Age	55
Sex	Female
Baseline Weight (kg)	49.5
Race	Caucasian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	10 Jan 2018
Event	1. Anorectal Infection 2. Sepsis 3. Relapse of MDS
Severity	1. Grade 3 2. Grade 5 3. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 03 Apr 2018 – 13 Apr 2018 2. 17 Apr 2018 – 23 May 2018 3. 23 May 2018 – 23 May 2018
Outcome Of Event	1. Resolved 2. Death 3. Death
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	23 May 2018

Narrative:
Patient GP3LAF-007 is a 55 year-old Caucasian female with Myelodysplastic Syndrome who received a Omidubicel transplant on 10-Jan-2018.

The patient was diagnosed with Myelodysplastic Syndrome (MDS) Refractory Anemia with excess blasts in transformation (RAEB-2) on 05-Jun-2017. She underwent induction therapy with FLAG-IDA and consolidation therapy with azacytidine (first cycle 16-Oct-2017 to 20-Oct-2017). Other medical history included endometriosis.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 78 mg/day for 3 days (5-Jan-2018 to 07-Jan-2018), thiotepa 270 mg/day for 2 days, (03-Jan-2018 to 04-Jan-2018), and busulfan 170 mg/day for 3 days (5-Jan-2018 to 07-Jan-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. She was on ciprofloxacin, fluconazole, posaconazole, and acyclovir for infection prophylaxis. Other medications included calcium and calcifediol. Neutrophil counts recovered at 35 days post-transplantation (14-Feb-2018). The patient was discharged from the hospital on 20-Feb-2018.

The patient was hospitalized for an anorectal infection from 03-Apr-2018 to 13-Apr-2018. She was readmitted on 17-Apr-2018 and a chest CT performed on 19-Apr-2018 showed a lung infection. The patient was transferred to the ICU due to sepsis on 14-May-2018. The source of sepsis was suspected to related to both anorectal and lung infections. The patient required noradrenaline and mechanical ventilation (orotracheal intubation). She had multi-organ failure due to sepsis, requiring intubation and hemodialysis. An echocardiogram was completed and endocarditis was suspected. On 16-May-2018, peripheral blood showed autologous lymphoid and myeloid chimerism. During her stay in the ICU, a BM exam was performed on 23-May-2018 which showed 15% blasts with dysplastic changes. The patient was diagnosed with relapse of MDS on 23-May-2018. The patient's condition worsened despite supportive and antibiotic treatment and she died on 23-May-2018. Primary cause of death was reported as sepsis, organism not identified. Autopsy was done.

Subject Identifier	GP3LAF-008
Age	51
Sex	Male
Baseline Weight (kg)	59.0
Race	Unknown
Study Therapy	Randomized to Omidubicel but received off-study Unmanipulated CBU transplant
Date Of Study Therapy Administration	23 Feb 2018
Event	Acute Myeloid Leukemia Relapse
Severity	Grade 5
Serious (Yes/no)	Yes
Start/stop date of Event	11 Jul 2018 - 17 Jul 2018
Outcome Of Event	Death
Relationship To The Study Drug	No
Date Of Death (If Applicable)	17 Jul 2018

Narrative:

Patient GP3LAF-008 is a 51 year-old race unknown, ethnicity unknown male with AML who was randomized but did not receive the study transplant per the randomized arm. The patient was withdrawn from the study prior to transplant and was followed for primary/secondary endpoints and survival. The patient received an off-study UCB transplant on 23-Feb-2018.

The patient was diagnosed with AML - Acute Myelomonocytic Leukemia (M4) on 15-Aug-2017. Induction therapy consisted of idarubicin 12 mg/m2/24 h x 3 days plus cytarabine 200 mg/m^2 and consolidation therapy consisted of mitoxantrone plus cytarabine for two cycles. The patient was in CR1 with no blasts or MRD at screening on 17-Jan-2018. Other medical history included hereditary spherocytosis diagnosed at 6 years old (throughout his life he had presented with hemolytic crises in relation to infections that resolved spontaneously with infection control) and moderate pulmonary impairment. He had no history of splenectomy.

The patient was withdrawn from the study prior to administration of the conditioning regimen. Conditioning regimen and concomitant medication data for the off-study transplant were not reported in the data system. The patient achieved neutrophil engraftment within the study protocol target windows.

The patient was admitted due to malaise on 11-Jul-2018 and acute myeloid leukemia Relapse was found. No further treatment was given. The patient passed away on 17-Jul-2018. Autopsy was not performed.

Subject Identifier	GP3LAF-009
Age	30
Sex	Male
Baseline Weight (kg)	78.0
Race	Caucasian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	14 May 2018
Event	1. Lung Infection 2. Soft Tissue Infection 3. Upper Respiratory Infection 4. Gastrointestinal Infection
Severity	1. Grade 3 2. Grade 4 3. Grade 2 4. Grade 2
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 25 May 2018 – 28 Jun 2018 2. 12 Jun 2018 – 28 Jun 2018 3. 15 Oct 2018 – 16 Oct 2018 4. 17 Dec 2018 – 18 Dec 2018
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LAF-009 is a 30 year-old Caucasian male with ALL who received a Unmanipulated CBU transplant on 14-May-2018.

The patient was diagnosed with ALL (subtype t(9;22) (q34;q11), BCR/ABL+) on 13-Nov-2017. He received induction and consolidation therapy with PETHEMA LLA-phi 2008 and Dasatinib. The patient's medical history included mild hepatic impairment, severe pulmonary dysfunction, and intestinal invagination which resolved spontaneously on 20-Oct-2017. Surgical history included appendectomy in March 2009.

Prior to UCB transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 100 mg/day (9-May-2018 to 11-May-2018), thiotepa 390 mg/day (7-May-2018 to 8-May-2018), and busulfan 250 mg/day (9-May-2018 to 11-May-2018). GvHD prophylaxis including mycophenolate mofetil and cyclosporine was started on 07-May-2018. Infection prophylaxis included fluconazole, voriconazole, Bactrim, ciprofloxacin, acyclovir, Posaconazole, and valacyclovir. Neutrophil counts recovered at 22 days post-transplantation (05-Jun-2018). The patient was discharged from the hospital on 28-Jun-2018.

The patient's post-transplantation period was complicated by a lung infection (25-May-2018) requiring supplemental oxygen. The lung infection was treated with IV antibiotics and antifungals. No microbial agent was identified. During the same hospitalization for transplant, the patient developed a soft tissue infection in his neck. An urgent CT was performed on 12-Jun-2018 which showed extensive edema in the retropharyngeal space, multiple right cervical adenopathies without abscess, thickening of the right internal jugular vein (suspicious for thrombophlebitis), and extension of inflammation/infection to the mediastinum. The patient required surgery and was transferred to the ICU.

The patient required emergent orotracheal intubation on 12-Jun-2018 to prevent airway compromise. The patient improved and was transferred from the ICU on 14-Jun-2018. He was still receiving IV antibiotics but was recovering at the time of transfer. The patient improved and was extubated and transferred to the Hematology Unit on 14-Jun-2018. The lung and neck soft tissue infections were reported as resolved as of 28-Jun-2018. The patient was later admitted for an upper respiratory infection from 15-Oct-2018 to 16-Oct-2018 and a gastrointestinal infection from 17-Dec-2018 to 18-Dec-2018. Both the upper respiratory and gastrointestinal infections resolved without sequelae.

Subject Identifier	GP3LAF-010
Age	60
Sex	Male
Baseline Weight (Kg)	64.0
Race	Unknown
Study Therapy	Omidubicel
Date Of Study Therapy Administration	24 Jan 2019
Event	Seizure
Severity	Grade 2
Serious (Yes/no)	Yes
Start/stop date of Event	24 Jan 2019 – 05 Feb 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	NA: Pre-Transplant Event
Date Of Death (If Applicable)	

Narrative:
Patient GP3LAF-010 is a 60 year-old male with AML who received a Omidubicel transplant on 24-Jan-2019.

The patient was diagnosed with AML on 24-Feb-2017. He underwent induction therapy with 3+7 PETHEMA LMA <65 (27-Feb-2017). Consolidation therapy included PETHEMA LMA 2010 <65 (idarubicin and cytarabine) starting on 29-Apr-2017 and PETHEMA LMA 2010 <65 (HiDAC) starting on 21-Jun-2017. The patient received an autologous peripheral blood hematopoietic stem cell transplantation on 31-Aug-2017. For the transplant he was treated with intravenous (IV) busulfan (12.8 mg/kg), etoposide (40 mg/kg), cytarabine (12 gr/m^2), and G-CSF priming (80 mcg). The patient then underwent reinduction therapy with two cycles of EC TPI-ALV-201 (alvocidib, mitoxantrone, and cytarabine) with cycle #1 starting on 09-Oct-2018 and cycle #2 starting on 21-Nov-2018. The patient's past medical history included renal agenesis and a traumatic subdural hematoma due to a motorcycle accident. The motorcycle accident resulted in C7, T8, clavicle, and rib fractures which required surgical intervention. The patient had moderate pulmonary impairment (DLCO 68%) at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (19-Jan-2019 to 21-Jan-2019), thiotepa (17-Jan-2019 to 18-Jan-2019), and busulfan (19-Jan-2019 to 21-Jan-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included fluconazole, voriconazole, ciprofloxacin, acyclovir, and posaconazole. Neutrophil counts recovered at 12 days post-transplantation (05-Feb-2019). The patient was discharged from the hospital on 05-Feb-2019.

The patient developed seizures hours before the Omidubicel transplantation on 24-Jan-2019. The episode was quickly controlled by diazepam IV and no further episodes were observed. A brain scan was performed which showed nothing remarkable. An MRI was also done and found a small subdural bleed. The cause of the seizures was not explained by these findings, and the most probable cause was considered likely related to cyclosporine/busulfan. The seizure event was considered resolved as of 05-Feb-2019.

Subject Identifier	GP3LAF-011

Age	36
Sex	Female
Baseline Weight (kg)	70.0
Race	Unknown
Study Therapy	Omidubicel
Date Of Study Therapy Administration	17 Jan 2019
Event	PGF
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	21 Feb 2019 – 15 Mar 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	Yes
Date Of Death (If Applicable)	

Narrative:
Patient GP3LAF-011 is a 36-year-old female with AML who received a Omidubicel transplant on 17-Jan-2019.

The patient was diagnosed with AML (minimally differentiated - M0) on 22-May-2018. She underwent induction therapy with EC AC220 (QUANTUM FIRST clinical trial) which included 3+7 and quizartinib/placebo starting on 23-May-2018. Due to disease resistance, another cycle of induction therapy with EC WO29519 was started on 05-Jul-2018. The site received permission from Gamida Cell for the patient to enroll in this clinical trial, as it was within 30 days of randomization. This induction cycle included five days of cytarabine 1 mg/m^2 and idasanutlin/placebo. The patient underwent consolidation therapy with cycle 1 starting on 14-Sep-2018 and cycle 2 starting on 19-Nov-2018. The patient had moderate/severe pulmonary impairment at study screening. Her surgical history included appendectomy.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 80 mg/day (12-Jan-2019 to 14-Jan-2019), thiotepa 290 mg/day (10-Jan-2019 to 11-Jan-2019), and busulfan 190 mg/day (12-Jan-2019 to 14-Jan-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included fluconazole, ciprofloxacin, acyclovir, and poscanazole.

The patient received a Omidubicel transplant on 17-Jan-2019. There were no shipping, storage, or infusion deviations except for a temperature excursion to 9.8ºC (acceptable range 2-8ºC) in the refrigerator containing the bags of infusion solution (the diluent used for Omidubicel cultured and uncultured fractions). The sponsor was aware and approved to use the products. Prior to infusion, acetaminophen, dexchlorpheniramine, and hydrocortisone were given per protocol. There were no infusion reactions.

A BM aspiration on 13-Feb-2019 showed no hematopoietic cells and chimerism 5% donor. HHV-6 infection was reported post-transplant (day 21: 690 copies/ml, day 28: 3024 copies/ml), however no treatment was provided. The patient was on acyclovir prophylaxis 500 mg/m^2 IV Q8hr starting day -7. The patient received G-CSF 300µg dose as per protocol. Methylprednisolone was given on days 26-28 for suspected skin GvHD (rash), however there was no suspicion of engraftment syndrome. The patient did not recover her neutrophil count. A BM aspirate performed on 20-Feb-2019 showed no hematopoietic cells. The patient was diagnosed with PGF on 21-Feb-2019.

The study center proceeded to treat the patient with a haploidentical transplant, and the conditioning regimen was started on 22-Feb-2019. The patient received a haploidentical transplant on 26-Feb-2019. She engrafted with ANC >500/mm3 as of 15-Mar-2019. There was no platelet recovery as of that date. Complete chimerism was noted after second transplantation (100% donor).

Subject Identifier	GP3LAF-012
Age	24
Sex	Male
Baseline Weight (kg)	76.0

Race	Unknown
Study Therapy	Omidubicel
Date Of Study Therapy Administration	11 Oct 2019
Event	1. Febrile Neutropenia 2. Lung Infection
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 23 Oct 2019 – 28 Oct 2019 2. 13 Apr 2020 – 22 Apr 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LAF-012 is a 24 year-old male with AML who received a Omidubicel transplant on 11-Oct-2019.

The patient was diagnosed with AML on 23-Apr-2019. He underwent induction therapy with 3 + 7 (25-Apr-2019), reinduction therapy with FLAG-Ida (28-Jun-2019), and consolidation therapy with HiDAC (04-Sep-2019). The patient's past medical history included positive *S. epidermidis* blood cultures (07-Aug-2019) and phimosis. He was a prior smoker. The patient had mild hepatic and moderate pulmonary impairment at study screening. His surgical history included tonsillectomy and surgical intervention for phimosis.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (06-Oct-2019 to 08-Oct-2019), thiotepa (04-Oct-2019 to 05-Oct-2019), and busulfan (06-Oct-2019 to 08-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included fluconazole, acyclovir, posaconazole, and ciprofloxacin. Neutrophil counts recovered at seven days post-transplantation (18-Oct-2019). The patient was discharged from the hospital on 21-Oct-2019.

The patient was admitted on 23-Oct-2019 due to febrile neutropenia. There was no clear source for the fever. He received treatment with intravenous (IV) antibiotics. The patient improved during hospitalization and was discharged on 28-Oct-2019.

The patient was then admitted on 13-Apr-2020 due to a lung infection. He received broad-spectrum treatment with piperacillin-tazobactam, hydroxychloroquine, and amphotericin B. COVID-19 tests were negative. Due to nephrotoxicity the amphotericin B was changed to isavuconazole. The patient was discharged home and the lung infection was considered resolved on 22-Apr-2020.

Subject Identifier	GP3LAF-013
Age	51
Sex	Female
Baseline Weight (kg)	56.0
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	13 Feb 2020
Event	Febrile Neutropenia
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	12 Dec 2019 – 20 Dec 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	NA: Pre-transplant event

Date Of Death (If Applicable)
Narrative: Patient GP3LAF-013 is a 51 year-old White female with AML who received an Unmanipulated CBU transplant on 13-Feb-2020. The patient was diagnosed with AML on 31-Jul-2019. She underwent induction therapy with two cycles of 3+7 (idarubicin and cytarabine) with quizartinib/placebo. She underwent one cycle of consolidation therapy with HiDAC. The patient was admitted for febrile neutropenia on 12-Dec-2019 following consolidation therapy. She improved with intravenous antibiotics and was discharged on 20-Dec-2019. The patient's past surgical history included tonsillectomy in childhood and surgical intervention for anorectal infection. Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (08-Feb-2020 to 10-Feb-2020), thiotepa (06-Feb-2020 to 07-Feb-2020), and busulfan (08-Feb-2020 to 10-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included fluconazole, voriconazole, ciprofloxacin, acyclovir, posaconazole, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 32 days post-transplantation (16-Mar-2020). The patient was discharged from the hospital on 06-Mar-2020.

Subject Identifier	GP3LOY-001
Age	39
Sex	Male
Baseline Weight (kg)	90.7
Race	White - Mediterranean
Study Therapy	Omidubicel
Date Of Study Therapy Administration	02 Dec 2017
Event	Toxoplasmosis Brain Infection
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	01 May 2018 – 14 Jan 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	
Narrative: Patient GP3LOY-001 is a 39 year-old White, Mediterranean male with AML who received a Omidubicel transplant on 02-Dec-2017. The patient was diagnosed with AML on 17-Apr-2017. He underwent induction therapy with HiDAC and Mitoxantrone (21-Apr-2017 to 27-Apr-2017) and consolidation therapy with HiDAC and sorafenib (cycle #1 31-May-2017, cycle #2 12-Jul-2017, cycle #3 21-Aug-2017, and off sorafenib 10-Sep-2017). The patient's past medical history included dilated aortic root (incidental finding on TEE on 15-Jun-2017), left kidney stones (2011), and right rotator cuff tear (2002). Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (27-Nov-2017 to 29-Nov-2017), thiotepa (25-Nov-2017 to 26-Nov-2017), and busulfan (27-Nov-2017 to 29-Nov-2017). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included fluconazole, levofloxacin, valacyclovir, and Posaconazole. Neutrophil counts recovered at 10 days post-transplantation (12-Dec-2017). The patient was discharged from the hospital on 22-Jan-2018. The patient fell on an outstretched hand and injured his right foot on 30-Apr-2018. X-ray of the hand showed no acute fracture or pathology from his fall. He had been increasingly altered and progressively slow to answer questions over the week prior to the fall. MRI of the brain on 02-May-2018 found a 2 cm enhancing mass within the left thalamus with surrounding vasogenic edema extending to the left midbrain and middle cerebellar peduncle. There was a resulting mass effect on the left lateral and third ventricles. On 04-May-2018 a CT head showed a stable left thalamic mass. Thalamic mass biopsy was positive for toxoplasmosis. The patient was	

started on pyrimethamine, sulfadiazine, and leucovorin for 6 weeks starting from 03-May-2018 to 15-Jun-2018. The patient was also found to have Metapneumovirus and enterocolitis secondary to Shiga-like toxin *E. Coli* and was given supportive care. X-ray of the right hand on 10-May-2018 was normal. The patient was discharged to acute rehab on 09-May-2018.

The patient was discharged from rehab on 18-May-2018. He was continued on pyrimethamine, sulfadiazine, and leucovorin. On 01-Jun-2018 CT head showed improvement in appearance of the left thalamic lesion with no evidence of midline shift. There was a residual area of low attenuation secondary to edema/ischemia. The patient's speech was improving and his was mentation clearer. He still reported right hand cramping and tremors. MRI on 14-Jan-2019 was unchanged and the patient continued taking toxoplasmosis medication. The toxoplasmosis brain infection was considered resolved by convention on 14-Jan-2019.

Subject Identifier	GP3LOY-002
Age	48
Sex	Male
Baseline Weight (kg)	101.5
Race	Black – African American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	02 Jan 2018
Event	1. BK Viremia 2. Dermatomal Zoster Infection
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 05 Mar 2018 – 13 Mar 2018 2. 02 Dec 2018 – 11 Dec 2018
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LOY-002 is a 48 year-old Black, African American male with AML who received an Unmanipulated CBU transplant on 02-Jan-2018.

The patient was diagnosed with AML on 01-Mar-2017. He underwent pre-induction therapy with Entospletinib (10-Mar-2017 to 24-Mar-2017) and induction therapy with one cycle of 7+3 Daunorubicin and Cytarabine (24-Mar-2017 to 30-Mar-2017) and cycle #1 of Entospletinib (24-Mar-2017 to 31-May-2017). He underwent consolidation therapy with HiDAC and Entospletinib (Entospletinib cycle #2: 01-Jun-217 to 30-Aug-2017; HiDAC cycle #1: 28-Apr-2017 to 03-May-2017; HiDAC cycle #2: 01-Jun-2017 to 06-Jun-2017; HiDAC cycle #3: 16-Aug-2017 to 21-Aug-2017). The patient's past medical history included a cavitary lung lesion being treated with Posaconazole (17-Sep-2017), periodontal disease and extraction of teeth numbers 17 and 32 (09-Mar-2017), and testicular epididymal cysts (20-Nov-2016). He used marijuana daily starting as a teenager with the last use reported as approximately 09-Aug-2017. He had severe pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (28-Dec-2017 to 30-Dec-2017), thiotepa (26-Dec-2017 to 27-Dec-2017), and busulfan (28-Dec-2017 to 30-Dec-2017). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included valacyclovir, acyclovir, Posaconazole, and levofloxacin. Neutrophil counts recovered at 16 days post-transplantation (18-Jan-2018). The patient was discharged from the hospital on 02-Feb-2018.

The patient was admitted on 05-Mar-2018 for management of BK viremia. The patient had been seen in clinic and complained of decreased urine output and hematuria. He was catheterized in clinic which improved urine output, but he was admitted for further management of BK viremia. Results of BK Virus DNA PCR serum on 27-Feb-2018 was 183 copies/ml and on 06-Mar-2018 was 610 copies/ml. IgG was 667 on 19-Feb-2018 and he received IVIG on 21-Feb-2018. During admission the patient received continuous bladder irrigation treatment. His foley was removed on 10-Mar-2018 and the urine returned clear. He had a course of AKI on 12-Mar-2018 with a creatinine of 1.61 mg/dl which improved with fluid resuscitation. The patient was discharged on 13-Mar-2018 with Tacrolimus 1 mg BID and continued Posaconazole, Valtrex, and Bactrim.

The patient was then admitted on 02-Dec-2018 with dermatomal zoster infection. Lesions had begun 5 days prior to admission and progressively spread. The patient presented with raised vesicles in a dermatomal distribution. He had no fevers or chills at the time. He was started on acyclovir 10 mg/kg TID. Skin VZV PCR was positive. The patient was monitored until the vesicles scabbed over and was then discharged home on valacyclovir on 11-Dec-2018.

Subject identifier	GP3LOY-003
Age	47
Sex	Female
Baseline weight (kg)	78.9
Race	Black – African American
Study therapy	Omidubicel
Date of study therapy administration	28 Sep 2018
Event	1. HHV6 Viremia 2. CMV Viremia 3. Herpes Zoster Virus 4. Relapsed T-Lymphoblastic Leukemia
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3
Serious (yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 20 Oct 2018 – 03 Dec 2018 2. 03 Jan 2019 – 18 Mar 2019 3. 18 Mar 2019 – 03 Apr 2019 4. 07 Jun 2019 – 25 Nov 2019
Outcome of event	1. Resolved 2. Resolved 3. Resolved 4. Resolved by convention
Relationship to the study drug	1. No 2. No 3. No 4. No
Date of death (if applicable)	23 May 2020

Narrative:
Participant GP3LOY-003 is a 47 year-old Black, African American female with Acute Lymphoblastic Leukemia who received an omidubicel transplant on 28-Sep-2018.

The participant was diagnosed with high-risk Acute Lymphoblastic Leukemia (Precursor T-cell ALL) on 07-Dec-2017. She underwent induction treatment with four cycles of hyper-CVAD (cycle #1: 19-Dec-2017, cycle #2: 26-Jan-2018, cycle #3: 26-Feb-2018, and cycle #4: 27-Mar-2018). The participant did not receive

consolidation or secondary therapy but received long-term therapy with two cycles of nelarabine (cycle #1: 11-Jun-2018, cycle #2: 09-Jul-2018). No re-induction or salvage therapy was given. The participant's past medical history included bilateral hand and feet neuropathy (01-Jun-2018), acute pancreatitis (related to peg asparaginase, 15-Apr-2018), Grave's disease (s/p radio ablation in 2011), hypothyroidism (25-Feb-2011, treated), folate deficiency (2010), idiopathic thrombocytopenic purpura (2006), vitamin B deficiency (2006), and migraines (Aug-2001). She also had mild hepatic and moderate pulmonary impairment at study screening. Surgical history included hysterectomy (Jul-2006) and appendectomy (Oct-1987).

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine 93 mg/day (23-Sep-2018 to 25-Sep-2018), thiotepa 373 mg/day (21-Sep-2018 to 22-Sep-2018), and busulfan 239 mg/day (23-Sep-2018 to 25-Sep-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included posaconazole, valacyclovir, and levofloxacin. Neutrophil counts recovered at 14 days post-transplantation (12-Oct-2018). The participant was discharged from the hospital on 14-Oct-2018.

Post-transplantation the participant was hospitalized for a Human herpesvirus 6 infection from 20-Oct-2018 to 25-Oct-2018. The HHV6 infection was considered resolved on 03-Dec-2018. She was then hospitalized for cytomegalovirus viremia from 03-Jan-2019 to 04-Jan-2019 and again from 14-Jan-2019 to 15-Jan-2019 (resolved on 18-Mar-2019). The participant was admitted for management of Herpes zoster infection from 18-Mar-2019 to 21-Mar-2019. The Herpes zoster virus infection was considered resolved on 03-Apr-2019.

The participant's study disease T-Lymphoblastic Leukemia then relapsed on 07-Jun-2019 (post-transplantation day +252). The participant's bone marrow showed 77% blasts. Treatment was started with cycle #1 nelarabine 1500mg/m2/dose given on 17-Jun-2019, 19-Jun-2019, and 21-Jun-2019 for relapsed disease. The participant did not receive the last dose of nelarabine due to neurotoxicity, which eventually resolved. Cycle #2 of nelarabine with cyclophosphamide was started on 08-Jul-2019, but treatment day 5 was held due to neurotoxicity. Chimerism sent on 17-Jul-2019 showed > 98% donor.

Bone marrow exam on 31-Jul-2019 then showed 70% blasts. There was no evidence of CNS relapse. Decitabine was started on 07-Aug-2019 and venetoclax was started on 08-Aug-2019. The plan was to give 4-6 cycles of treatment. Bone marrow flow cytometry on 03-Sep-2019 showed some residual disease. Bone marrow from 07-Oct-2019 showed residual disease with 1% involvement. The participant was seen on 25-Nov-2019 for her 15-month follow-up scheduled visit. At the time she was receiving cycle #4 of her treatment with decitabine and venetoclax, with the most recent course given on 06-Nov-2019. The leukemia relapse event was considered resolved by convention on 25-Nov-2019 as the participant completed her study follow up.

On 04-Mar-2020, a biopsy of the right tonsil revealed Monomorphic Post-Transplant Lymphoproliferative Disorder (PTLD), Diffuse Large B-Cell Lymphoma (activated B-cell type) post-transplantation day +523). A biopsy of a gastric ulcer on 25-Mar-2020 also showed PTLD. The PTLD was treated with rituximab initially and subsequently with lenalidomide, cyclophosphamide, dexamethasone, ibrutinib, and brentuximab. Despite treatment, the PTLD progressed. The participant died on 23-May-2020 with the primary cause of death reported as PTLD (post-transplantation day +603). Secondary causes of death included bacterial infection and respiratory, hepatic, and renal failure.

Subject identifier	GP3LOY-004
Age	49
Sex	Female
Baseline weight (kg)	51.8
Race	White-Mediterranean
Study therapy	Unmanipulated CBU
Date of study therapy administration	11 Oct 2018
Event	No Serious Adverse Events Reported

Severity
Serious (yes/no)
Start/stop date of Event
Outcome of event
Relationship to the study drug
Date of death (if applicable)
Narrative: Participant GP3LOY-004 is a 49 year-old White-Mediterranean female with Lymphoma who received an unmanipulated cord blood unit transplant on 11-Oct-2018. The participant was diagnosed with Lymphoma on 17-Apr-2018. She underwent treatment with six cycles of ESHAP chemotherapy (cycle #1: 07-May-2018, cycle #2: 29-May-2018, cycle #3: 18-Jun-2018, cycle #4: 09-Jul-2018, cycle #5: Jul-2018, and cycle #6: Aug-2018). The participant's medical history included moderate pulmonary impairment at study screening. Prior to unmanipulated cord blood unit transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine (06-Oct-2018 to 08-Oct-2018), thiotepa (04-Oct-2018 to 05-Oct-2018), and busulfan (06-Oct-2018 to 08-Oct-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, posaconazole, valacyclovir, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 24 days post-transplantation (04-Nov-2018). The participant was discharged from the hospital on 03-Nov-2018. Minimal residual disease was detected in the bone marrow following the transplant confirming disease relapse on 08-May-2020. Therapy was initiated on 30-May-2020 with lenalidomide. Therapy was held the first week of August 2020 due to pancytopenia. The participant received tazemetostat from 29-Dec-2020 through 22-Feb-2021. A bone marrow exam performed on 24-Feb-2021 revealed some abnormal lymphocytes (45%) and blast cells (4%) consistent with involvement of the participant's known T-cell lymphoma. Two cycles of romidepsin (09-Mar-2021 and 06-Apr-2021) were administered, and a PET scan on 12-May-2021 showed a complete remission – no scintigraphic evidence of FDG avid lymphoma. No further treatment has been administered. As of 25-Aug-2021, the participant is alive with no reports of any subsequent disease relapses.

Subject Identifier	GP3LOY-005
Age	44
Sex	Female
Baseline Weight (kg)	127.5
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	16 Jan 2019
Event	1. HHV6 encephalitis 2. HSV Esophagitis 3. Failure to Thrive 4. Gastric Perforation 5. Septic Shock
Severity	1. Grade 4 2. Grade 3 3. Grade 3 4. Grade 4 5. Grade 4
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 02 Feb 2019 – 04 Mar 2019

	2. 26 Feb 2019 – 20 Mar 2019 3. 18 Oct 2019 – 16 Jan 2020 4. 07 Nov 2019 – 20 Dec 2019 5. 07 Nov 2019 – 27 Nov 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No 5. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LOY-005 is a 44 year-old White female with AML who received an Unmanipulated CBU transplant on 16-Jan-2019.

The patient was diagnosed with AML (with maturation - M2) on 21-Nov-2014. She underwent induction therapy with 7+3 Cytarabine and daunorubicin (24-Nov-2014 to 30-Nov-2014) and consolidation therapy with four cycles of HiDAC (cycle #1: 26-Dec-2014, cycle #2: 22-Jan-2015, cycle #3: 23-Feb-2015, and cycle #4: 06-Apr-2015). After relapse she underwent induction with 7+3 Cytarabine and daunorubicin (13-Nov-2017 to 19-Nov-2017), reinduction with HiDAC with IT-methotrexate (16-Jan-2018 to 19-Jan-2018), and consolidation with two cycles of HiDAC (cycle #1: 19-Mar-2018, cycle #2: 30-Jul-2018).

The patient's past medical history included hirsutism (1989), impaired fasting glucose (16-Jul-2014), polycystic ovarian syndrome (18-Aug-2014), PICC related thrombus (May-2015), uterine fibroids (2016), sleep apnea (06-Jun-2016), Type II diabetes mellitus (20-Jul-2016), dyslipidemia (Aug-2016), vitamin D deficiency (Aug-2016), choledocholithiasis (12-Oct-2017), acute biliary pancreatitis (12-Oct-2017), perisplenic mass (Oct-2017), acute cholecystitis (07-Feb-2018), and anisometropia of the right eye (29-May-2018). Relevant medical history present at screening included cardiac impairment (11-Dec-2018: calculated LVEF of 40% via MUGA scan), moderate/severe hepatic impairment, severe pulmonary impairment, obesity, depression (2015), and anxiety (2015). Surgical history included bilateral sphincterotomy (Oct-2017), pancreatic duct stent removal (26-Oct-2017), common bile duct stent and pancreatic stent placement (2017), and cholecystectomy (2018). The patient had a reported allergy to allopurinol (2014) and tramadol (2014).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 93 mg/day (11-Jan-2019 to 13-Jan-2019), thiotepa 397 mg/day (09-Jan-2019 to 10-Jan-2019), and busulfan 240 mg/day (11-Jan-2019 to 13-Jan-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, acyclovir, posaconazole, and valacyclovir. Neutrophil counts recovered at 19 days post-transplantation (04-Feb-2019).

The patient's post-transplantation course was complicated by fatigue, diarrhea, *E. coli* bacteremia, and severe protein-calorie malnutrition. Her labs showed increasing serum C02 and an arterial blood gas (ABG) with mild but compensated hypercarbia. She was placed on BiPAP but had increasing fatigue and work of breathing. On the morning of 02-Feb-2019, the patient had worsening mental status (lethargy) with hypoventilation and an ABG of 7.28/88. She was unable to protect her airway. Infectious workup included blood, urine, and bronchoalveolar lavage cultures. She was started on meropenem. The patient was intubated for acute hypercapnic respiratory failure and placed on AC/VC ventilation. CSF Meningitis PCR panel was positive for HHV6 on 05-Feb-2019. She was extubated on 06-Feb-2019 and placed on nasal cannula 3 L oxygen. She was started on ganciclovir 600 mg Q12hrs on 07-Feb-2019. She became afebrile after starting ganciclovir. As of 08-Feb-2019, there was no history of dyspnea, nausea, or vomiting. She was tolerating tube feedings and her diarrhea was improving.

A repeat CSF Meningitis PCR panel on 20-Feb-2019 was negative for HHV6. Ganciclovir was stopped on 27-Feb-2019 and oral valganciclovir was started. Valganciclovir was stopped on 04-Mar-2019. The HHV6 encephalitis event was reported as resolved without sequelae as of 04-Mar-2019. The hospitalization was further prolonged because the patient developed HSV esophagitis (26-Feb-2019 to 20-Mar-2019). The HSV esophagitis was complicated by poor oral intake requiring Dobhoff tube placement. The patient was discharged home on 20-Mar-2019 with Dobhoff tube in place for home tube feedings.

The patient was then admitted for failure to thrive on 18-Oct-2019. The patient had an unsuccessful PEG placement attempt on 30-Oct-2019 with Gastroenterology. She was noted to have pneumoperitoneum on CT abdomen/pelvis on 31-Oct-2019. The patient then underwent PEG placement surgery on 04-Nov-2019. Shortly after starting tube feeds, the patient developed worsening acute abdominal pain and shock. A bedside ultrasound of the abdomen was obtained and showed moderate intra-abdominal free fluid around the liver and within the pelvis. CT abdomen/pelvis was positive for contrast extravasation.

The patient required emergent management of gastric perforation on 07-Nov-2019. The patient was taken back to the operating room on 07-Nov-2019 for exploratory laparotomy, abdominal washout, removal of PEG tube, gastric wedge resection, and AbThera placement as negative pressure therapy. A static abdominal ultrasound showed free fluid around the liver and pelvis. The patient was taken to the surgically ill ICU (SICU) post-operation to manage recurrent septic shock and was intubated and sedated for increasing pressor requirements. The patient was treated with fluid resuscitation, vasopressor management (dexmedetomidine, epinephrine, norepinephrine, phenylephrine, propofol, and vasopressin), antibiotics (meropenem, IV vancomycin, nystatin, IV valacyclovir, IV voriconazole, sulfamethoxazole-trimethoprim, and biotene mouth rinse), and 1 L normal saline bolus for lactic acidosis.

On 09-Nov-2019, the patient was taken back to the operating room for washout and closure. The patient was treated with Zosyn and received aggressive diuresis. She remained hemodynamically stable without the use of vasopressors. The treating team considered the septic shock event to be resolved with no residual effects on 27-Nov-2019. The patient continued to have a complicated course during her admission but was clinically stable for discharge home on 20-Dec-2019. Average blood pressures at discharge were 122/78 and blood cultures were no growth to date. The patient was discharged to a rehab facility and was still receiving TPN and tube feeds. She was discharged home from rehab on 20-Jan-2020 with PT, OT, and home health nurse.

Subject Identifier	GP3LOY-006
Age	61
Sex	Male
Baseline Weight (kg)	47.6
Race	Asian - Indian/South Asian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	22 Feb 2019
Event	1. Coronavirus Upper Respiratory Tract Infection 2. Adenovirus Pneumonia 3. Bronchospasm 4. Human Metapneumovirus URI
Severity	1. Grade 3 2. Grade 3 3. Grade 4 4. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 21 Apr 2019 – 08 May 2019 2. 02 May 2019 – 08 May 2019 3. 03 May 2019 – 04 May 2019

	4. 27 Dec 2019 – 30 Dec 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LOY-006 is a 61 year-old Indian/South Asian male with AML who received a Omidubicel transplant on 22-Feb-2019.

The patient was diagnosed with AML with myelodysplasia related changes (deletion 7) on 24-Sep-2018. He underwent induction therapy with one cycle of daunorubicin/Cytarabine liposome (Vyxeos) from 19-Oct-2018 to 23-Oct-2018. The patient's past medical history included hyperlipidemia, hypertension, severe protein-calorie malnutrition (Nov-2018), and giardia stool infection (Nov-2018). He had severe pulmonary impairment at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 75 mg/day (17-Feb-2019 to 19-Feb-2019), thiotepa 250 mg/day (15-Feb-2019 to 16-Feb-2019), and busulfan 160 mg/day (17-Feb-2019 to 19-Feb-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included posaconazole, valacyclovir, and levofloxacin. Neutrophil counts recovered at 7 days post-transplantation (01-Mar-2019). The patient was discharged from the hospital on 05-Mar-2019.

The patient was admitted on 21-Apr-2019 with fever, cough, tachycardia, and leukocytosis and was subsequently diagnosed with a Coronavirus upper respiratory tract infection. He was discharged on 22-Apr-2019 and then readmitted on 02-May-2019 for persistent cough. Coronavirus was positive on respiratory viral panel (RVP) on 22-Apr-2019 and 29-Apr-2019. CT chest on 02-May-2019 showed a worsening left lower lobe nodular tree-in-bud pattern from presumed viral pneumonia. The patient underwent a bronchoscopy on 03-May-2019. The bronchoscopy was complicated by bronchospasm which required emergency intubation but did not require administration of pressors. The patient had a breathing trial and was successfully extubated on 04-May-2019. Bronchoalveolar lavage studies were positive for adenovirus and Coronavirus. Lung biopsy was negative for CMV, adenovirus, fungal organisms, granulomas, or malignancy. BNP had been elevated on admission, but transthoracic echo showed no signs of volume overload. The patient received IVIG on 06-May-2019. Repeat chest X-ray on 06-May-2019 showed near complete resolution of the left lower lobe opacities. The patient was discharged on 08-May-2019 with a 14-day course of Levaquin to complete. He was breathing comfortably on room air on day of discharge.

The patient was then admitted for management of a human Metapneumovirus upper respiratory tract infection on 27-Dec-2019. RVP had been positive for human Metapneumovirus on 23-Dec-2019 and when repeated on 27-Dec-2019. A chest X-ray on 27-Dec-2019 showed hyperinflated lung fields with slightly increased patchy opacities and nodularity of the lung bases. Duo nebs had been given every four hours and Advair every 12 hours in the 24 hours prior to admission without improvement. The patient was treated with ceftriaxone and azithromycin on 27-Dec-2019 which were later switched to Levaquin and azithromycin on 29-Dec-2019. Prednisone 40 mg daily for 2 days was started on 28-Dec-2019. The human Metapneumovirus URI was considered resolved on 30-Dec-2019.

Subject identifier	GP3LOY-007
Age	42
Sex	Female
Baseline weight (kg)	99.4

Race	White
Study therapy	Omidubicel
Date of study therapy administration	06 Mar 2019
Event	1. HHV6 Viremia 2. Acute Kidney Injury
Severity	1. Grade 3 2. Grade 3
Serious (yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 30 Mar 2019 – 12 Apr 2019 2. 13 May 2019 – 22 May 2019
Outcome of event	1. Resolved 2. Resolved
Relationship to the study drug	1. No 2. No
Date of death (if applicable)	25 Dec 2020

Narrative:
Participant GP3LOY-007 is a 42 year-old White female with Acute Myelogenous Leukemia who received an omidubicel transplant on 06-Mar-2019.

The participant was diagnosed with Acute Myelogenous Leukemia on 18-Jun-2018. She underwent induction therapy with one cycle of daunorubicin, cytarabine, and mitostaurin (RYDAP; 20-Jun-2018 to 15-Jul-2018), consolidation therapy with one cycle of high dose cytarabine and mitostaurin (27-Aug-2018 to 31-Aug-2018) and 2 GY radiation therapy for biopsy positive left forearm skin lesion (25-Oct-2018 to 13-Nov-2018), and reinduction therapy with one cycle of daunorubicin/cytarabine liposome (Vyxeos; 26-Nov-2018 to 30-Nov-2018). The participant's past medical history included right upper thrombus near her peripherally inserted central catheter (PICC) (Jun-2018) and two episodes of kidney stones (Jul-2007 and Jun-2006). She had mild hepatic impairment at study screening. The participant had a reported allergy to cefepime (Jun-2018).

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine (01-Mar-2019 to 03-Mar-2019), thiotepa (27-Feb-2019 to 28-Feb-2019), and busulfan (01-Mar-2019 to 03-Mar-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, acyclovir, and posaconazole. Neutrophil counts recovered at eight days post-transplantation (14-Mar-2019). The participant was discharged from the hospital on 18-Mar-2019.

The participant was admitted for initiation of intravenous (IV) foscarnet for HHV6 viremia on 30-Mar-2019. Routine surveillance of HHV6 levels on 20-Mar-2019 had been notable at 5,830 copies/mL. The participant was discharged on 01-Apr-2019 on IV foscarnet. She completed foscarnet on 12-Apr-2019. The participant's baseline creatine was 1.1 mg/dL and was up to 2.74 mg/dL on 09-May-2019. The participant was then admitted for acute kidney injury (AKI) with a creatinine of 4.99 mg/dL on 13-May-2019. Foscarnet had been on hold since 09-May-2019 due to hyperkalemia and negative HHV6. Tacrolimus had been stopped a week prior due to AKI. Bladder scan on admission showed minimal urine. The participant was discharged on 22-May-2019 at which point the participant's creatinine had improved to 1.49 mg/dL.

The site did not report this participant's disease relapse as an SAE, but since the protocol defined relapse as a medically important event, the information has been provided.

The day +100 study-related bone marrow performed on 19-Jun-2019 showed 1% blasts with 40% cellularity. Flow cytometry did not show a significant increase in the blast population. A fine needle aspirate skin biopsy of a lesion on the participant's right thigh performed on 27-Jun-2019 revealed the presence of highly atypical cells suspicious for malignancy. Additional biopsies were done on 10-Jul-2019 of skin lesions located on the left shin and right thigh. The findings supported the diagnosis of focal involvement by acute myeloid leukemia in a panniculitic distribution.

Local radiation was given as treatment. A total dose of 30 Gy in 15 fractions was administered to the anterior lateral skin of the participant's right thigh using the electron beam technique from 16-Sep-2019 to 04-Oct-2019.

A bone marrow exam performed on 27-Feb-2020 showed no evidence of leukemia. The participant experienced a biopsy proven extramedullary relapse of disease (leukemia cutis) on 08-May-2020. Treatment was administered with a total of 24 Gy radiotherapy divided in 12 fractions. Gilteritinib was also started on 28-May-2020; however, new lesions appeared and the existing lesion were noted to be enlarged. The radiotherapy and gilteritinib were discontinued. Three cycles of azacitidine and venetoclax were started on 25-Jun-2020 and the third cycle was given on 20-Aug-2020. A bone marrow exam performed on 27-Aug-2020 showed no evidence of leukemia, but the extramedullary disease was noted to have progressed again and subcutaneous cytarabine was initiated without benefit. Hydroxyurea and venetoclax were started. Additional radiotherapy was given to the remaining lesions in late September 2020. On 12-Nov-2020 the participant's leukemia progressed and a lumbar puncture (LP) was consistent with leukemic meningitis. Intrathecal chemotherapy was given as treatment as well as systemic cytarabine and radiotherapy to her lumbar spine. Repeat LPs continued to show aggressive recurrence of the leukemia but a bone marrow biopsy performed on 23-Nov-2020 was without evidence of leukemia.

The participant died on 25-Dec-2020 with the primary cause of death being disease relapse. Secondary causes of death included bacterial and viral infections.

Subject Identifier	GP3LOY-008
Age	50
Sex	Male
Baseline Weight (kg)	99.2
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	20 May 2019
Event	1. HHV6 Viremia 2. Herpes Zoster
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 06 Jul 2019 – 10 Jul 2019 2. 06 Nov 2019 – 09 Jan 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LOY-008 is a 50 year-old White male with CML who received a Omidubicel transplant on 20-May-2019.

The patient was diagnosed with CML on 15-May-2012. He underwent induction therapy with imatinib 400 mg PO QD (May-2012 to Dec-2015), dasatinib 100 mg PO QD (Dec-2015 to Nov-2016), and hydrea (06-Oct-2016), maintenance therapy with nilotinib 400 mg PO BID (Jan-2016 to Dec-2017, Jul-2018 to Dec-2018) and Bosutinib 500 mg PO QD (Dec-2018 to Jan-2019), and reinduction therapy with HiDAC and Mitoxantrone (15-May-2018 to 20-May-2018) and EC therapy (22-Jun-2018 to 17-Jul-2018). The patient's past medical history included hypertension and hypercholesterolemia. He had moderate pulmonary impairment at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (15-May-2019 to 17-May-2019), thiotepa (13-May-2019 to 14-May-2019), and busulfan (15-May-2019 to 17-May-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, posaconazole, and levofloxacin. Neutrophil counts recovered at 11 days post-transplantation (31-May-2019). The patient was discharged from the transplant hospitalization on 29-Jun-2019.

The patient was diagnosed with HHV6 viremia (PCR 4,630) on 03-Jun-2019. HHV6 levels on 10-Jun-2019 were 31,600 after 3-4 days of ganciclovir. Ganciclovir 5mg/kg BID (07-Jun-2019 to 15-Jun-2019) was switched to foscarnet on 15-Jun-2015 due to affect changes. Foscarnet was then discontinued on 23-Jun-2019 and switched to valacyclovir 1 gm TID. HHV6 levels from 22-Jun-2019 were negative, however the virus reactivated on 29-Jun-2019 (PCR 2920). Given increasing virus titers the patient was admitted on 06-Jul-2019 to restart foscarnet (dose 70 mg/kg q12h based on current renal function). The patient was alert and oriented x 3 on admission. HHV6 levels were negative on 10-Jul-2019 at which point the HHV6 viremia event was considered resolved.

The patient was then admitted for fevers (emergency room [ER] temp of 100.9) and a rash concerning for shingles on 06-Nov-2019. The Herpes Zoster infection was limited to the coccygeal region along the S1 dermatome. The patient was treated with IV acyclovir. The shingles resolved and the patient was discharged on 09-Jan-2020.

Subject Identifier	GP3LOY-009
Age	22
Sex	Male
Baseline Weight (kg)	74.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	24 Jun 2019
Event	1. Gastrointestinal Symptoms 2. Gastrointestinal Symptoms
Severity	1. Grade 3 2. Grade 2
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 03 Aug 2019 – 07 Aug 2019 2. 31 Aug 2019 – 12 Sep 219
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3LOY-009 is a 22 year-old White, Hispanic or Latino male with AML who received an Unmanipulated CBU transplant on 24-Jun-2019.

The patient was diagnosed with AML on 22-Feb-2019. He underwent induction therapy with one cycle of daunorubicin, cytarabine, and mitostaurin (26-Feb-2019 to 21-Mar-2019) and consolidation therapy with one cycle of HiDAC with mitostaurin (15-Apr-2019 to 28-Apr-2019). The patient had moderate pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (19-Jun-2019 to 21-Jun-2019), thiotepa (17-Jun-2019 to 18-Jun-2019), and busulfan (19-Jun-2019 to 21-Jun-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection

prophylaxis included levofloxacin, valacyclovir, and posaconazole. Neutrophil counts recovered at 17 days post-transplantation (11-Jul-2019). The patient was discharged from the hospital on 11-Jul-2019.

The patient presented with nausea and vomiting on 03-Aug-2019. The gastrointestinal symptoms effected his ability to tolerate his immunosuppressive medications. On admission his infectious workup (chest x-ray, blood culture, stool PCR) was negative. The patient was unable to afford olanzapine outpatient which was rectified by the case manager. He was restarted on olanzapine and had scheduled ondansetron (Zofran) which resolved his symptoms overnight. Given his improvement with loperamide, the patient was discharged, and the event was considered resolved on 07-Aug-2019. The patient then had poor appetite for several weeks starting 31-Aug-2019, with severe nausea and vomiting for one day with blood-tinged emesis. He had no ongoing signs of bleeding and his hemoglobin was stable. The gastrointestinal symptoms were considered resolved on 12-Sep-2019.

Subject Identifier	GP3LOY-010
Age	50
Sex	Female
Baseline Weight (kg)	91.7
Race	Black – African
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	30 Dec 2019
Event	1. Gram-Negative Bacteremia 2. Fluid Overload 3. Septic Shock
Severity	1. Grade 3 2. Grade 4 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 29 Jan 2020 – 03 Feb 2020 2. 13 Feb 2020 – 06 Apr 2020 3. 22 Feb 2020 – 06 Apr 2020
Outcome Of Event	1. Resolved 2. Death 3. Death
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	06 Apr 2020

Narrative:
Patient GP3LOY-010 is a 50 year-old Black, African female with ALL who received an Unmanipulated CBU transplant on 30-Dec-2019.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor B-Cell ALL) on 02-Jan-2019. She underwent induction treatment with three cycles of hyper-CVAD (04-Jan-2019 to 14-Jun-2019). The disease relapsed and the patient went on to receive reinduction/salvage therapy with vincristine, methotrexate, dexamethasone, and mercaptopurine (26-Jul-2019 to 05-Aug-2019.) She received a CD19 CAR-T-cell infusion on 19-Aug-2019. The patient's past medical history included diabetes and latent tuberculosis (January 2019). She had severe pulmonary impairment (cDLCO: 64%) at study screening. Surgical history included cesarean section (1999). The patient had reported drug allergies to chloroquine and ceftriaxone.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of thiotepa 355 mg/day (23-Dec-2019 to 24-Dec-2019), busulfan 227 mg/day (25-Dec-2019 to 27-Dec-2019), and fludarabine 90 mg/day (25-Dec-2019 to 27-Dec-2019). GvHD prophylaxis included

mycophenolate mofetil (MMF) and tacrolimus. Infection prophylaxis included posaconazole, valacyclovir, trimethoprim-sulfamethoxazole, and levofloxacin. Neutrophil counts recovered at 14 days post-transplantation (13-Jan-2020). The patient was discharged from the hospital on 23-Jan-2020.

The patient was admitted from clinic for a fever of 100.9ºF on 28-Jan-2020. Blood cultures were obtained and grew gram-negative rods. Treatment included one liter of normal saline and meropenem. Antibiotic coverage was changed to levofloxacin on 01-Feb-2020 and continued through 12-Feb-2020. The patient was discharged from the hospital on 03-Feb-2020.

A tacrolimus level was noted to be supratherapeutic on 10-Feb-2020 (17.8 ng/mL). Over the next few days, the patient's weight increased by 30 pounds. Other issues included an elevated BNP to 709 mg/dL, increased creatinine to 2.0 mg/dL, severe hyponatremia related to hypervolemia, and complaints of dyspnea on exertion. The patient was admitted on 13-Feb-2020 for management of tacrolimus-induced fluid overload and acute liver injury. Treatment was initiated with intravenous diuretics, norepinephrine, fluid restriction, and tacrolimus discontinuation. The patient was also treated with defibrotide as her presentation was suspicious for VOD.

On 19-Feb-2020, the patient was evaluated for persistent constipation and was given laxatives and GoLytely without therapeutic effect. On 21-Feb-2020, a CT of the abdomen and pelvis revealed a small bowel obstruction. The patient acutely deteriorated overnight on 21-Feb-2020 requiring increasing pressor support with the addition of vasopressin. Given the clinical picture of GI distension and intrabdominal pressure, the patient was treated for distributive shock. Blood cultures were drawn on 22-Feb-2020, and cefepime and flagyl were started for empiric gram-negative and anaerobic coverage. Repeat abdominal imaging on 28-Feb-2020 revealed that the small bowel obstruction had resolved.

The patient continued to decline and required intubation due to altered mental status and respiratory failure. The clinical picture was consistent with metabolic encephalopathy. A CT of the head was obtained and negative for abnormalities. Norepinephrine was added for pressure support. Blood cultures obtained on 22-Feb-2020 grew *Bacteroides fragilis* in one of two sets. Meropenem was added for coverage. A stress dose of steroids was started and MMF was discontinued. The patient continued to require ventilation support and pressor support. Blood urea nitrogen (BUN) and creatinine levels peaked on 04-Mar-2020 (BUN: 139 mg/dL, creatinine: 4.84 mg/dL) and then decreased to 29 mg/dL and 0.81 mg/dL, respectively, on 29-Mar-2020.

On 23-Mar-2020, the patient had a noticeable drop in hemoglobin and was noted to have hematochezia and blood streaks in her stool. The gastroenterology service was consulted to evaluate for a gastrointestinal bleed. The patient was evaluated for hemolysis and labs were positive, so the consultants felt this was likely the source for the drop in hemoglobin. The patient was treated with blood product transfusions and aminocaproic acid (Amicar).

On 27-Mar-2020, a code blue was called for the patient due to bradycardia, hypotension, and hypoxia. The patient recovered with intervention but continued to require intensive care with ventilation support and four vasopressors to maintain hemodynamic stability. Per the recommendation of nephrology, CVVH was started for the patient's worsening acidosis, and increase in BUN and creatinine. Antibiotic coverage was expanded to include vancomycin, cefepime, and metronidazole. COVID-19 testing was performed and negative. The patient continued to require maximal medical interventions without improvement. The patient expired on 06-Apr-2020. Primary cause of death was noted as septic shock and secondary causes noted as multi-organ failure and toxic metabolic encephalopathy. An autopsy was not done.

Subject Identifier	GP3LOY-011
Age	64
Sex	Male
Baseline Weight (Kg)	91.0
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	11 Oct 2019

Event	1. Respiratory Distress 2. Septic Shock
Severity	1. Grade 4 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 29 Oct 2019 – 02 Nov 2019 2. 01 Nov 2019 – 02 Nov 2019
Outcome Of Event	1. Death 2. Death
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	02 Nov 2019

Narrative:
Patient GP3LOY-011 is a 64 year-old White male with AML who received an Unmanipulated CBU transplant on 11-Oct-2019.

The patient was diagnosed with AML (Acute myelomonocytic leukemia (M4) with cerebrospinal fluid involvement) on 07-Mar-2019. He underwent induction therapy with leukapheresis (09-Mar-2019), hydroxyurea (10-Mar-2019 to 12-Mar-2019), 6 cycles of azacitidine and venetoclax (08-Apr-2019 to 15-Sep-2019), and intrathecal methotrexate (15-Mar-2019, 29-Mar-2019, 03-Apr-2019, 09-Apr-2019, 13-Apr-2019, 25-Apr-2019, 03-May-2019, 10-May-2019, 24-May-2019, 08-Jul-2019, 09-Aug-2019, and 09-Sep-2019). The patient did not receive consolidation, maintenance, or salvage therapy. The patient's past medical history included stage III chronic kidney disease, continuous veno-venous hemofiltration (CVVH in Mar-2019), hyperlipidemia, superficial thrombosis of bilateral cephalic veins (Mar-2019), RUL pulmonary embolism (Aug-2019), and QTc prolongation. The patient had previously been intubated (09-Mar-2019 to 11-Mar-2019) for acute hypoxic respiratory failure likely due to fluid overload. Surgical history included right frontal Ommaya reservoir placement (28-Mar-2019). He had a reported allergy to clarithromycin.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 102 mg/day (06-Oct-2019 to 08-Oct-2019), thiotepa 400 mg/day (04-Oct-2019 to 05-Oct-2019), and busulfan 272 mg/day (06-Oct-2019 to 08-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir. Neutrophil counts did not recover.

Post-transplantation the patient was severely immunocompromised. Along with his primary disease he had neutropenic fever, neutropenic colitis, Clostridium difficile diarrhea, paroxysmal atrial fibrillation, bacteremia, thrombocytopenia, and neutropenia. He had four confirmed infections involving blood/buffy coat: Streptococcus (14-Oct-2019), Enterobacter (14-Oct-2019), Enterococcus (17-Oct-2019), and HHV6 (25-Oct-2019). The multiple organism bacteremia and HHV6 encephalitis were treated with broad-spectrum antibiotics and foscarnet.

The patient's mental status declined. A head CT on 28-Oct-2019 was negative. There was an episode of vomiting with aspiration on 28-Oct-2019 after which a large bore nasogastric tube (NGT) was placed. The patient was intubated on 29-Oct-2019 due to his inability to protect his airway. The patient had abdominal distention and ongoing diarrhea (>1500 mL). CT scan of the abdomen suggested colitis and enteritis. No GvHD was diagnosed or treated.

The patient developed septic shock on 01-Nov-2019. He had increasing metabolic acidosis due to lactic acidosis, despite bicarbonate infusion and ventilator compensation. The septic shock was likely due to ongoing infections, particularly HHV6 involving meninges and CSF (23,8000 copies/mL on 25-Oct-2019 and 7610 copies/mL on 01-Nov-2019). The patient's status continued to worsen. He had atrial fibrillation with rapid ventricular rate and associated hypotension requiring amiodarone infusion. The patient was treated with amiodarone, sodium bicarbonate (started 01-Nov-2019), norepinephrine IV, and ventilator compensation, in addition to ongoing anti-bacterial, anti-viral, and anti-fungal treatment.

The patient went into asystole and passed away on 02-Nov-2019. Primary cause of death was noted as septic shock. Autopsy was not performed.

Deviations with potential medical significance: Busulfan and fludarabine were dosed using actual body weight/body surface area instead of ideal body weight/body surface area as mandated in the protocol in this patient's case. This resulted in busulfan and fludarabine over-dosing.

Subject Identifier	GP3LOY-012
Age	48
Sex	Female
Baseline Weight (kg)	95.1
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	31 Jan 2020
Event	1. GI GvHD Flare 2. Septic Shock
Severity	1. Grade 3 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 05 May 2020 – 19 Jul 2020 2. 14 Jul 2020 – 19 Jul 2020
Outcome Of Event	1. Death 2. Death
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	19 Jul 2020

Narrative:
Patient GP3LOY-012 is a 48 year-old White female with AML who received an Unmanipulated CBU transplant on 31-Jan-2020.

The patient was diagnosed with AML with MLL rearrangement on 15-Jul-2019. Induction therapy with daunorubicin and cytarabine was given from 17-Jul-2019 to 23-Jul-2019. The second and third cycles of induction with filgrastim, cladribine, and cytarabine were given from 30-Jul-2019 to 03-Aug-2019 and 14-Aug-2019 to 18-Aug-2019. The patient also received consolidation therapy with HiDAC from 15-Oct-2019 to 19-Oct-2019, 29-Nov-2019 to 03-Dec-2019, and 31-Dec-2019 to 03-Jan-2020. The patient's past medical history included depression and anxiety (1993), diabetes, obesity, asthma, hypertension, hyperlipidemia, and tobacco use. She had severe pulmonary impairment (cDLCO = 64%) at study screening. Surgical history included a cholecystectomy, hysterectomy, left knee surgery, and a left femur shaft fracture. The patient had reported allergies to varenicline (Chantix), penicillin, and chlorhexidine.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of thiotepa 357 mg/day (24-Jan-2020 to 25-Jan-2020), fludarabine 90 mg/day (26-Jan-2020 to 28-Jan-2020), and busulfan 228 mg/day (26-Jan-2020 to 28-Jan-2020). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, trimethoprim-sulfamethoxazole, valganciclovir, and posaconazole. Neutrophil counts recovered at 14 days post-transplantation (14-Feb-2020). The patient was discharged from the hospital on 06-Mar-2020.

The post-transplant course was complicated by GvHD diagnosed via sigmoidoscopy in February 2020. The GvHD was treated with intravenous (IV) methylprednisolone which was tapered with oral budesonide. Stool PCR on 28-Apr-2020 was negative for infection. The patient was admitted to the hospital on 05-May-2020 for increased bowel movements over the previous three days. The patient reported two to three large, watery stools, increased gas, cramping, and incontinence. She denied abdominal pain outside of the bowel movements. She

also complained of decreased appetite, fatigue, and weight loss. No nausea, vomiting, fever, chills, or rash were reported. The patient was admitted for workup and treatment. She was made nothing by mouth (NPO) and started on TPN for nutritional support. Methylprednisolone dose was adjusted to 1 mg/kg twice daily. A repeat flexible sigmoidoscopy was performed on 06-May-2020 which showed congested, erythematous, nodular, and ulcerated mucosa in the rectum, sigmoid colon, and descending colon. A colonoscopy performed on 01-Jul-2020 showed numerous significant ulcerations, some of which were bleeding. Concurrent to the GI GvHD flare, the patient was also being treated for CMV viremia (she had a history of CMV colitis) and possible CMV pneumonitis. Despite treatment, she still had positive CMV PCR levels. In addition, the patient was on antibiotics for new onset typhlitis (neutropenic enterocolitis). The typhlitis was related to the GvHD of the colon but predated her recent GvHD deterioration.

On 14-Jul-2020, the patient became extremely short of breath and required ~80% oxygen via high-flow nasal cannula. Oxygen requirements increased to 100% high-flow nasal cannula the following day and BiPAP by 16-Jul-2020. The patient was intubated on 17-Jul-2020 for hypercapnia, hypoxia, and change in mental status. She developed shock post-intubation. On 19-Jul-2020, the patient was on maximum pressor support (norepinephrine, phenylephrine, and vasopressin) and had systolic blood pressures in the 50s via arterial line. She was on pressure control at this point and assist-control with spontaneous respirations giving her 700 mL tidal volume, but her respiratory rate did not correspond with the amount of acidosis.

Per physician report, the etiology of the worsening shock was unclear. The patient also developed worsening renal failure, becoming anuric and hyperkalemic with cardiotoxicity which ultimately descended into cardiac arrest. The patient died on 19-Jul-2020. Primary cause of death was septic shock. Secondary cause of death was noted as multi-organ failure and GvHD. Autopsy was not done.

Subject Identifier	GP3MAN-001
Age	13
Sex	Male
Baseline Weight (kg)	45.5
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	26 Jul 2019
Event	1. Patient Anxiety Due to Treatment 2. Anemia 3. TMA – Requiring Admission
Severity	1. Grade 3 2. Grade 3 3. Grade 1
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 01 Aug 2019 – 13 Aug 2019 2. 19 Dec 2019 – 21 Dec 2019 3. 13 Apr 2020 – 08 Jul 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved by convention
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	
Narrative: Patient GP3MAN-001 is a 13 year-old White male with ALL who received an Unmanipulated CBU transplant on 26-Jul-2019.	

The patient was diagnosed with Precursor T-cell ALL with CNS involvement on 10-Dec-2012. Induction therapy with regimen B was started on 13-Dec-2012. This was escalated to regimen C consolidation on 30-Jan-2013 due to the presence of MRD on Day 29, making the disease high-risk. Delayed intensification was initiated on 12-Jun-2013 followed by 12 cycles of maintenance therapy with dexamethasone, vincristine, mercaptopurine, methotrexate, and co-trimoxazole (07-Aug-2013 to 17-Apr-2016). Disease relapse was confirmed on 10-Mar-2019. Reinduction therapy with mitoxantrone, methotrexate, dexamethasone, and vincristine was started on 12-Mar-2019. The patient's past medical history included behavioral issues for which psychology was involved and central line Staphylococcal infection (16-Mar-2019). He had mild-severe hepatic impairment (elevated bilirubin April 2019) and severe pulmonary impairment (cDLCO 60%) present at study screening. Surgical history included central line placements.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 35 mg/day (19-Jul-2019 to 21-Jul-2019), cyclophosphamide 2880 mg/day (19-Jul-2019 to 20-Jul-2019), and TBI 200 cGy (22-Jul-2019 to 25-Jul-2019). GvHD prophylaxis included mycophenolate mofetil (MMF) and cyclosporine. Infection prophylaxis included penicillin, acyclovir, and itraconazole. Neutrophil counts recovered at 25 days post-transplantation (20-Aug-2019). The patient was discharged from the hospital on 02-Oct-2019.

During the acute post-transplant period, the patient had an episode of anxiety/non-compliance on 01-Aug-2019. He would not allow staff to administer the afternoon dose of MMF on 31-Jul-2019 which escalated the next day to not allowing any medications or blood products to be given. Psychology was notified but the patient would not engage with them. A care conference was held during which a plan to give midazolam sedation was agreed upon to allow the patient to relax and allow medications to be given as prescribed. The first dose of midazolam was administered on 02-Aug-2019 but was not enough to sedate and relax the patient. The number of staff required to support the patient could no longer be sustained so he was transferred to the ICU to continue treatment. In the ICU he was given midazolam, clonidine, and chloral hydrate over the course of the day. He was eventually intubated due to the sedation. On 10-Aug-2019, the patient was extubated. Sedatives were continued but he was more compliant during the rest of his stay in the ICU. The patient was transferred back to the transplant unit on 13-Aug-2019.

The patient was seen in clinic on 18-Dec-2019 for routine lab work but was noted to have upper respiratory symptoms prompting a nasal swab. Based on the results of his hemoglobin, platelets, and bilirubin, he returned to clinic on 19-Dec-2019 for transfusions given suspected hemolytic anemia. The patient developed a fever during the transfusion and was admitted per institutional policy. Blood cultures were negative, and he was discharged on 21-Dec-2019.

The respiratory panel from 18-Dec-2019 revealed RSV which resulted in an atypical hemolytic uremic syndrome (HUS). The patient's renal function slowly began to normalize and no treatment was indicated. However, his creatinine levels and his Cystatin C levels slowly increased. The patient was admitted on 13-Apr-2020 for further investigation and a renal biopsy as advised by the renal team. The patient underwent the biopsy on 14-Apr-2020 and was discharged home. Results revealed glomeruli with numerous red cells and fibrin thrombi. There was also interstitial fibrosis and tubular atrophy involving approximately 10-15% of the sample supporting a diagnosis of thrombotic microangiopathy (TMA).

The patient continued regular follow ups as an outpatient. His creatinine remained high (maximum of 158 umol/L on 08-Apr-2020) with an improvement in urea (7.9 mmol/L on 12-Jun-2020). The urine protein creatinine ratio in April decreased to 23 and was within normal limits at the 12-Jun-2020 visit. Blood pressure remained stable at 118/88 as well. The consensus among the consultants was that the TMA was probably secondary to the underlying oncological diagnosis and corresponding treatment. They did not believe it was a sign of primary complement driven acute HUS. Therefore, treatment with eculizumab was not recommended. The thrombotic microangiopathy was considered resolved by convention as it remained persistent at study completion.

Subject Identifier	GP3NUH-001

Age	38
Sex	Female
Baseline Weight (kg)	42.8
Race	Asian - Filipino
Study Therapy	Omidubicel
Date Of Study Therapy Administration	05 Jun 2018
Event	1. CMV Reactivation 2. Viral Illness 3. Fever
Severity	1. Grade 1 2. Grade 1 3. Grade 2
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 03 Jul 2018 – 06 Jul 2018 2. 02 Aug 2018 – 13 Aug 2018 3. 28 Aug 2018 – 04 Sep 2018
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3NUH-001 is a 38 year-old Asian, Filipino female with ALL who received a Omidubicel transplant on 05-Jun-2018.

The patient was diagnosed with ALL on 27-Nov-2017. She underwent induction therapy with hyper-CVAD cycle 1A starting on 30-Nov-2017, with 100 mg once a day (OD) dasatinib given for 14 days, methotrexate starting on 11-Dec-2017, and cytarabine starting on 27-Dec-2017. Induction hyper-CVAD cycle 1B started on 03-Jan-2018 with 70 mg OD dasatinib given continuously. The patient's past medical history included iron deficiency and incidental right para-uterine vein thrombosis. She had positive CMV status at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (31-May-2018 to 02-Jun-2018), thiotepa (29-May-2018 to 30-Jun-2018), and busulfan (31-May-2018 to 02-Jun-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, trimethoprim-sulfamethoxazole, ciprofloxacin, fluconazole, piperacillin-tazobactam, and posaconazole. Neutrophil counts recovered at 6 days post-transplantation (11-Jun-2018). The patient was discharged from the hospital on 27-Jun-2018.

The patient was admitted for fever and loose stools on 04-Jul-2018. She was found to be CMV positive and was started on valganciclovir. On 06-Jul-2018 the patient was discharged. She was afebrile at discharge. The patient was then admitted on 02-Aug-2018 with a viral illness. On 04-Aug-2018 she was found to have non-tender, non-pruritic rashes on her palms and soles, as well as dry oral mucosa. Dermatology consult on 06-Aug-2018 described the rashes as confluent, non-follicular discreet papules involving the soles and extending to the proximal thighs, the palms extending proximally, and a small amount scattered over the anterior chest. There were no blisters seen and no oral mucosa or facial involvement was reported. The rash on the palms improved on 07-Aug-2018 and the rash over the palms and soles improved on 08-Aug-2018. The palm rash resolved on 11-Aug-2018. CMV DNA was <590 copies. EBV and HHV 6 were not detected. Respiratory multiplex was positive for enterovirus and rhinovirus. On 14-Aug-2018, the patient was afebrile, the rash over the hands and feet was stable, and the patient was discharged.

The patient was then admitted on 28-Aug-2018 with 3 days of fever (maximum temperature of 38°C), diarrhea, and poor appetite. She also reported 3 days of dysphagia, feeling that water would get stuck going down, and associated intermittent chest tightness and odynophagia. She denied respiratory or urinary symptoms, headache, nausea, or vomiting. CXR on 29-Aug-2018 showed no consolidations or pleural effusion. Blood and urinary tests were negative. Stool C. difficile toxin test was negative. On 31-Aug-2018 the patient was afebrile and vitals were stable. The patient had epigastric pain and continued to have diarrhea on 01-Sep-2018. On 03-Sep-2018 stool frequency decreased but the consistency was still watery. On 04-Sep-2018 the patient was afebrile and hemodynamically stable, and the patient was discharged.

Subject Identifier	GP3NUH-002
Age	38
Sex	Female
Baseline Weight (kg)	75.1
Race	Asian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	24 Jul 2019
Event	1. CMV Infection 2. Chickenpox 3. Pneumonia 4. Pneumonia 5. Pneumonia
Severity	1. Grade 2 2. Grade 3 3. Grade 3 4. Grade 3 5. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 09 Sep 2019 – 27 Sep 2019 2. 09 Dec 2019 – 31 Dec 2019 3. 03 Mar 2020 – 18 Mar 2020 4. 01 Apr 2020 – 08 Apr 2020 5. 11 May 2020 – 15 May 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No 5. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3NUH-002 is a 38 year-old Asian female with CML who received a Omidubicel transplant on 24-Jul-2019.

The patient was diagnosed with CML on 02-Oct-2018. She underwent treatment with nilotinib 400 mg BD (12-Oct-2018), dasatinib 140 mg for 2 months (18-Jan-2019), and ponatinib 45 mg (20-Mar-2019). The

patient's past medical history also included incomplete miscarriage, hemolytic anemia, and left groin hematoma. She had severe pulmonary impairment at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (19-Jul-2019 to 21-Jul-2019), thiotepa (17-Jul-2019 to 18-Jul-2019), and busulfan (18-Jul-2019 to 20-Jul-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included trimethoprim-sulfamethoxazole, acyclovir, micafungin, ciprofloxacin, and posaconazole. Neutrophil counts recovered at 12 days post-transplantation (05-Aug-2019). The patient was discharged from the hospital on 04-Sep-2019.

The patient was admitted for CMV treatment on 09-Sep-2019. Her counts were still low at that time and were considered too fragile for ganciclovir. The CMV viral load was 1200 IU/mL on 11-Sep-2019, 430 IU/mL on 18-Sep-2019, and <180 IU/mL on 25-Sep-2019. The patient was discharged on 27-Sep-2019. The CMV infection was noted as persisting on 30-Sep-2019.

The patient then developed erythema and itching on the left upper limb on 03-Dec-2019. The skin findings generalized and developed into vesicles the following day. The patient was admitted on 10-Dec-2019 for likely disseminated zoster despite the patient's compliance with prophylaxis acyclovir. On 22-Dec-2019 the patient developed Type 1 Respiratory Failure and she was transferred to the MICU. The patient was stable on 31-Dec-2019 when she was discharged.

On 03-Mar-2020, the patient was found to have a fever in clinic. Her vitals at the time were T 38.6, BP 143/87, HR 115, and RR 28. The patient reported having a cough with whitish sputum for one week and a sore throat that had improved. The patient was diagnosed with community-acquired pneumonia on 04-Mar-2020. Chest X-ray showed airspace opacities in the left lower lobe and new patchy mass-like opacification of the right mid to upper zones. COVID-19 swabs were negative. CT thorax on 10-Mar-2020 showed multiple scattered pulmonary nodules, some with cavitation and some with suggestion of a faint halo of ground-glass change. In the given clinical context, atypical infections were considered. Acid-fast bacillus smear was positive from bronchoalveolar lavage on 11-Mar-2020. Respiratory culture grew Pseudomonas sensitive to ciprofloxacin and IV piperacillin-tazobactam. Treatment was given with piperacillin-tazobactam from 09-Mar-2019 to 14-Mar-2019 and changed to oral ciprofloxacin on 15-Mar-2019. MRI brain on 13-Mar-2020 showed no acute intracranial abnormality or enhancement. The patient was discharged in stable condition on 18-Mar-2020.

The patient was then admitted on 01-Apr-2020 after she was found to be febrile. Blood cultures, urine cultures, and chest x-rays (when compared to prior admission) were with non-significant findings. COVID-19 swabs were negative. CT thorax on 06-Apr-2020 showed previously noted multifocal areas of nodular consolidation. Most of the areas had improved relative to the CT on 10-Mar-2020, but there were new extensive areas of confluent consolidation in the right lower lobe, nodular densities in the posterior RUL, and patchy airspace changes in the lingula possibly consistent with bronchiolitis obliterans organizing pneumonia. The patient remained clinically well with no fevers or desaturations. She was discharged on 08-Apr-2020 with plans to wean prednisolone outpatient.

The patient was then again admitted on 11-May-2020 when she was incidentally found to be febrile prior to an outpatient CT thorax. She was asymptomatic at the time. Blood cultures, urine cultures, and nasal swabs were insignificant. CT thorax on 13-May-2020 found bilateral inflammatory lung opacities which showed a mix of partially improved disease and new sites of disease. The patient was stable and discharged on 15-May-2020.

Subject Identifier	GP3NUH-004
Age	31
Sex	Female
Baseline Weight (kg)	49.2
Race	Asian - Chinese
Study Therapy	Unmanipulated CBU

Date Of Study Therapy Administration	19 Nov 2019
Event	1. Tacrolimus-Induced Transplant-Related Microangiopathy 2. Pyrexia Secondary to IVIG infusion
Severity	1. Grade 3 2. Grade 1
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 14 Jan 2020 – 22 Jan 2020 2. 04 Mar 2020 – 05 Mar 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3NUH-004 is a 31 year-old Asian, Chinese female with ALL who received an Unmanipulated CBU transplant on 19-Nov-2019.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor B-Cell ALL) on 15-Jan-2019. She underwent induction therapy with one cycle of MASPORE (vincristine sulfate, L-asparaginase, and methotrexate; 17-Jan-2019 to 22-Feb-2019), two cycles of MASPORE (cyclophosphamide, cytarabine, vincristine sulfate, and methotrexate; 05-Mar-2019 to 19-Mar-2019 and 10-May-2019 to 24-May-2019), intrathecal methotrexate (04-Apr-2019), two cycles of high-dose methotrexate (04-Apr-2019 to 18-Apr-2019), one cycle of FLAD (fludarabine phosphate, cytarabine, daunorubicin, and methotrexate); 28-Jun-2019 to 30-Jun-2019, and CAR-T infusion (fludarabine phosphate and cyclophosphamide; 14-Aug-2019 to 19-Aug-2019). The patient's past medical history included alpha thalassemia, migraine with aura (somatosensory, brainstem) with catamenial component (at time of ovulation and menses), gastroesophageal reflux disease, right ankle instability, and right hemorrhagic corpus luteum. She had moderate pulmonary impairment at study screening. The patient had reported allergies to amoxicillin/clavulanic acid.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 75 mg/day (14-Nov-2019 to 16-Nov-2019), thiotepa 245 mg/day (12-Nov-2019 to 13-Nov-2019), and busulfan 158 mg/day (14-Nov-2019 to 16-Nov-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, ciprofloxacin, posaconazole, and cotrimoxazole. Neutrophil counts recovered at 32 days post-transplantation (21-Dec-2019). The patient was discharged from the hospital on 01-Jan-2020.

On 14-Jan-2020, the patient was admitted from an outpatient clinic for concerns of thrombotic microangiopathy (TMA), likely induced from tacrolimus. The patient was being monitored for hyperbilirubinemia, rising lactate dehydrogenase (LDH), and red cell fragments for two weeks prior to the admission. In the clinic, the patient's blood pressure was 152/107. Labs indicated a hemoglobin of 8.4 g/dL, platelets of 11 x 10^9, and an elevated LDH of 2033 U/L. The patient was also noted to have an elevated creatinine of 101 µmol/L and decreased magnesium of 0.57 mmol/L, both attributed to tacrolimus. Tacrolimus level was 11.8 µg/L.

Upon admission, the patient's tacrolimus was held and the mycophenolate mofetil dose was changed to 750 mg three times daily. Further laboratory testing for Heinz Bodies was negative, so dapsone was not the likely cause for the TMA. However, the decision was made to hold dapsone. The patient received four units of platelets. Intravenous fluids (IV) were given to improve kidney function and IV magnesium was administered until TMA improved. Pentamidine by nebulizer was given in lieu of dapsone. Labs significantly improved with platelets increasing to 61 x 10^9 and LDH decreasing to 999 U/L. The patient was discharged in stable condition on 22-Jan-2020.

The patient was then admitted from clinic on 04-Mar-2020 for a fever that began during IVIG infusion. The patient had been feeling well prior to the IVIG infusion. During the infusion she felt feverish and had chills with mild chest tightness, shortness of breath, and nausea. The patient was asymptomatic on 05-Mar-2020 at which point the infusion reaction was considered resolved.

Subject Identifier	GP3NWU-001
Age	62
Sex	Female
Baseline Weight (Kg)	77.1
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	12 Dec 2019
Event	1. BK Viruria 2. *Staph epidermidis* Bacteremia 3. Platelet Count Decreased
Severity	1. Grade 2 2. Grade 3 3. Grade 4
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 23 Jan 2020 – 12 Mar 2020 2. 21 Feb 2020 – 24 Feb 2020 3. 28 Jul 2020 – 18 Aug 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3NWU-001 is a 62 year-old White female with AML who received a Omidubicel transplant on 12-Dec-2019.

The patient was diagnosed with secondary AML (derived from JAK2+ myeloproliferative neoplasm, not otherwise specified, diagnosed on 07-May-2018) on 25-Jul-2019. She underwent induction therapy with 7+3 with daunorubicin 60 mg/m^2 (01-Aug-2019) and consolidation therapy with one cycle of HiDAC 3 g/m^2 (21-Sep-2019). The patient's past medical history included sinus Aspergillus (05-Dec-2019), pulmonary embolism (08-Oct-2019), intermittent leukocytosis (25-Jul-2019), anemia (16-Nov-2018), uveitis (15-Oct-2018), sarcoidosis (Sep-2018), Kikuchi's syndrome (05-Jan-2018), positive lupus anticoagulant (07-Jul-2015), palpitations (15-Jan-2013), fibromyalgia (30-Jun-2011), and rheumatoid arthritis (30-Jun-2011). She had moderate pulmonary impairment at study screening. Surgical history included removal of two benign lung nodules (18-Jan-2017), oophorectomy (left-1987, right-1990), and tonsillectomy (childhood).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 80 mg/day (07-Dec-2019 to 09-Dec-2019), thiotepa 304 mg/day (05-Dec-2019 to 06-Dec-2019), and busulfan 195 mg/day (07-Dec-2019 to 09-Dec-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, posaconazole, micafungin, pentamidine, amphotericin B, levofloxacin, and valacyclovir. Neutrophil counts recovered at 28 days post-transplantation (09-Jan-2020). The patient was discharged from the hospital on 13-Jan-2020.

The patient was admitted from clinic on 23-Jan-2020 with dysuria, flank pain, nausea, and vomiting. The patient had developed dysuria and urinary frequency on 19-Jan-2020 and was started on nitrofurantoin for a

presumed UTI. Urine culture was positive for large blood but came back indeterminate secondary to contamination. The patient's symptoms persisted, and she was seen in clinic on 21-Jan-2020. Repeat urinalysis was positive for nitrates, small leukocyte esterase, and moderate blood. Repeat urine culture was negative for growth and she was continued on nitrofurantoin.

The patient developed left flank pain for approximately one hour on the night of 22-Jan-2020. She had worsening dysuria, a feeling of incomplete bladder emptying, and one episode of vomiting. The flank pain resolved with acetaminophen and did not return. She was admitted for further workup and imaging. A urine sample from 21-Jan-2020 was found to be positive for BK virus with 2.4 million copies/mL. The patient was treated with empiric cefepime from 23-Jan-2020 to 25-Jan-2020. She received an infusion of mesna 3500 mg/day from 24-Jan-2020 to 26-Jan-2020. The infusion was stopped due to lack of improvement. The patient was started on prophylactic ciprofloxacin on 25-Jan-2020. The patient was discharged in stable condition on 27-Jan-2020. She endorsed dysuria and hematuria at discharge.

The patient then presented to the ED on 21-Feb-2020 after blood cultures from 20-Feb-2020 were found to be positive for gram positive cocci. The patient reported intermittent fever for two days with a maximum temperature of 100.7°F just before she came to the hospital. She endorsed continued suprapubic pain, dysuria, and hematuria for which she was already receiving treatment for BK virus hemorrhagic cystitis.

Blood cultures on 20-Feb-2020 and 21-Feb-2020 were found to be positive for *Staphylococcus epidermidis* bacteremia. The patient was discharged on 24-Feb-2020 in stable condition. She was to continue oral linezolid 600 mg orally twice a day for a total of 14 days through 06-Mar-2020. Subsequent cultures since 22-Feb-2020 showed no growth. The BK viruria event was considered resolved as of 12-Mar-2020.

The patient then presented for a clinic visit and received a platelet transfusion on 22-Jul-2020. She tolerated the transfusion well until she returned for a post-platelet count at which time she complained of a throbbing headache and chills. She denied hives, shortness of breath, or rigors. A platelet transfusion reaction assessment was negative, but a platelet antibody panel sent on 22-Jul-2020 showed five reactive wells out of 13. The patient's headache was controlled with around the clock acetaminophen, but she did have notable mild photophobia. Since the reaction, she reported significant fatigue and decreased activity tolerance.

The patient presented to the ED on 28-Jul-2020 with a persistent throbbing headache and notable Grade 4 thrombocytopenia. Per the investigator, the event was thought to be likely immune-mediated thrombocytopenia given negative BM biopsies. Viral studies on 28-Jul-2020 were negative. CT brain without contrast showed no acute findings. The patient's platelet counts improved, and the patient was stable and discharged home on 01-Aug-2020 with intermittent headaches.

The platelet antibody screen from 22-Jul-2020 was not compatible with 22 random donors and showed 0% compatibility and later compatibility with one of 14 random donors tests, indicating approximately 7% compatibility. The HLA class I platelet antibody test sent on 29-Jul-2020 was negative. These results indicate alloimmune refractoriness toward platelet specific antigens, but not HLA antigens. A platelet ID panel performed on a sample from 28-Jul-2020 showed reactions to glycoprotein IIb/IIIA without identified specificity. Further specificity testing was sent on 18-Aug-2020 to identify if this was a platelet autoantibody or alloantibody against a high frequency platelet antigen. The decreased platelet count event was considered resolved as of 18-Aug-2020 when the platelet count was recovered back to 221,000 cells/L.

Subject Identifier	GP3NWU-002
Age	32
Sex	Male
Baseline Weight (kg)	80.0
Race	Asian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	17 Mar 2020
Event	1. Migraine Headache

	2. PGF 3. Multi-Organ Failure
Severity	1. Grade 3 2. Grade 4 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 30 Jan 2020 – 31 Jan 2020 2. 17 Apr 2020 – 02 May 2020 3. 31 Aug 2020 – 13 Sep 2020
Outcome Of Event	1. Resolved 2. Resolved with sequelae 3. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. Yes 3. No
Date Of Death (If Applicable)	13 Sep 2020

Narrative:
Patient GP3NWU-002 is a 32 year-old Asian male with AML who received a Omidubicel transplant on 17-Mar-2020. Of note, the product failed the release specifications of $\geq$ 8.0 x 10^8 total number of viable cells (TNC) for the cultured fraction, with a final result of 6.5 x 10^8. Therefore, the product was infused under special FDA permission at the request of the Investigator.

The patient was diagnosed with AML (Ph+ AML) on 10-Jun-2019. He underwent induction therapy with 7+3 (daunorubicin and cytarabine) on 21-Jun-2019, with dasatinib on days 8-21. He received consolidation therapy with two cycles of HiDAC starting 01-Aug-2019 (cycle 1) and 05-Sep-2019 (cycle 2), with dasatinib on days 6-26. Maintenance therapy included dasatinib (07-Aug-2019 to 23-Jan-2020) and ponatinib (29-Jan-2020). The patient's past medical history included intermittent headaches (ongoing) with hospitalization for migraines (30-Jan-2020), proctitis/rectal abscess (Jul-2019), myositis of the left lower triceps (07-Jul-2019 to 20-Jul-2019), attention deficit disorder, irritable bowel syndrome, gastroesophageal reflux disease, and blepharitis. Surgical history included fistulectomy (21-Aug-2019).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 96 mg/day (12-Mar-2020 to 14-Mar-2020), thiotepa 368 mg/day (10-Mar-2020 to 11-Mar-2020), and busulfan 236 mg/day (12-Mar-2020 to 14-Mar-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, levofloxacin, fluconazole, micafungin, pentamidine, and valacyclovir. The patient was diagnosed with *C. difficile* infection (16-Mar-2020) treated with vancomycin, BK viruria (28-Mar-2020), as well as a HHV6 viremia (23,900 copies/mL on 01-Apr-2020) treated with foscarnet during the transplant hospitalization. Filgrastim was initiated on 18-Mar-2020 at a dose of 300 mcg once per day, subcutaneously. The filgrastim dose was increased to 480 mcg starting on 03-Apr-2020. Neutrophil counts did not recover post-transplantation.

The patient remained pancytopenic post-transplantation without signs of engraftment. Peripheral blood chimerism on 07-Apr-2020 showed 100% donor. A BM biopsy was performed on 13-Apr-2020 which was hypocellular (<10% cellularity) with markedly decreased multilineage hematopoiesis and no increased blasts. Molecular studies on this aspirate were positive for BCR-ABL+ fusion transcript but below the level of quantification. Bone marrow chimerism showed no donor cells. He went on to receive a haploidentical SCT on 22-Apr-2020, and engraftment was confirmed on 04-May-2020.

The patient developed fevers on 16-Apr-2020, and blood cultures grew out *Stenotrophomonas maltophilia* (peripherally and from peripherally inserted central catheter (PICC) line). The site investigator confirmed PGF via BM exam on 17-Apr-2020.

While still admitted and preparing for a second transplant on 21-Apr-2020, the patient returned from a liver ultrasound and was noted to be febrile and hypoxic with 84% SaO_2 on room air. He was placed on oxygen via nasal cannula, but the oxygen saturation only recovered to approximately 90%. The patient denied shortness of breath but reported continued restrictive breathing, with an inability to take a full deep breath. Physical exam revealed slight crackles on the left side and rhonchi on the right side anteriorly. Nebulizer treatment with levalbuterol was administered with minimal effect, so a venturi mask was placed at 50% FiO_2 with resultant saturations in the range of 90-93%. A bedside chest X-ray revealed hazy infiltrates bilaterally suspicious for pneumonia as well as new, mild pulmonary edema. The patient continued to be febrile (102-103°F), tachycardic, and tachypneic (RR 28) with blood pressures within normal limits. A 100% non-rebreather mask was applied, and the patient was transferred to the ICU on 21-Apr-2020 for respiratory failure with febrile neutropenia and sepsis.

The patient received a T-cell depleted haploidentical stem cell infusion as planned on 22-Apr-2020 following ATG without conditioning in an effort to restore hematopoiesis. The patient eventually engrafted on 04-May-2020 but again became pancytopenic. Workup was consistent with secondary graft failure. The patient then received haploidentical CD34+ stem cells on 03-Jun-2020 following ATG and rituximab. The clinical course was complicated by HSV viremia and esophagitis concerning for multi-drug resistance, as well as *Stenotrophomonas* UTI and epididymitis.

The patient engrafted his WBCs but again became pancytopenic with workup consistent secondary graft failure. A BM biopsy performed on 29-Jul-2020 was negative for morphological evidence of relapse but was BCR/ABL positive (0.017%) after being negative peripherally one month prior on 27-Jun-2020. He did not receive specific treatment for the molecular relapse. A T-cell predominant DLI was administered on 30-Jul-2020. On 31-Jul-2020, the patient began spiking fevers again with intermittent episodes of hypoxia. He was found to have Methicillin-Resistant *Staphylococcus epidermidis* (MRSE), recurrent *Stenotrophomonas* bacteremia, and a worsening pneumonia. The patient subsequently developed a recurrent MRSE bacteremia and a *Candida krusei* fungemia.

Another haploidentical CD34+ cell infusion was administered on 04-Aug-2020. Filgrastim was given daily starting on 09-Aug-2020. The patient's immune suppression was completely discontinued on 30-Aug-2020. The patient received the remaining CD3+ cells on 31-Aug-2020 in hopes of eliciting WBC recovery. However, the patient's clinical status continued to deteriorate including multiple active infections with no evidence of WBC recovery and worsening respiratory status with increasing oxygen requirement. The patient passed away on 13-Sep-2020. Primary cause of death was noted to be multi-organ failure with a secondary cause being multiple infections/sepsis. An autopsy was not performed.

Subject Identifier	GP3OHS-001
Age	58
Sex	Female
Baseline Weight (kg)	50.3
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	26 Apr 2019
Event	1. GI GvHD 2. Staph Bacteremia 3. Left Femoral Neck Fracture 4. Pulmonary Embolism 5. Dysphagia
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3 5. Grade 3
Serious (Yes/no)	1. Yes

	2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 30 May 2019 – 17 Jun 2019 2. 23 Jul 2019 – 03 Sep 2019 3. 04 Oct 2019 – 15 Oct 2019 4. 17 Oct 2019 – 19 Oct 2019 5. 08 May 2020 – 16 May 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved with sequelae 4. Resolved with sequelae 5. Resolved
Relationship To The Study Drug	1. Yes 2. No 3. No 4. No 5. No
Date Of Death (If Applicable)	

Narrative:

Patient GP3OHS-001 is a 58 year-old White female with AML who received a Omidubicel transplant on 26-Apr-2019.

The patient was diagnosed with AML (without maturation - M1) on 19-Nov-2018. She underwent induction therapy with seven days of cytarabine (100 mg/m^2) and three days of idarubicin (12 mg/m^2) (23-Nov-2018 to 29-Nov-2018) and consolidation therapy with two cycles of HiDAC (cycle #1: 03-Jan-2019 to 08-Jan-2019, cycle #2: 31-Jan-2019 to 04-Feb-2019). The patient's past medical history included anxiety, panic disorder, deep vein thrombosis, gastroesophageal reflux disease, and psoriasis. She had moderate pulmonary impairment at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (22-Apr-2019 to 25-Apr-2019), fludarabine 38 mg/day (19-Apr-2019 to 21-Apr-2019), and cyclophosphamide 3300 mg/day (19-Apr-2019 to 20-Apr-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included trimethoprim-sulfamethoxazole, levofloxacin, valacyclovir, and posaconazole. Neutrophil counts recovered at 15 days post-transplantation (11-May-2019). The patient's post-transplantation hospitalization was complicated by pancytopenia and chemotherapy-induced nausea, vomiting, and diarrhea. The patient was discharged from the hospital on 19-May-2019.

The patient presented to the clinic on 30-May-2019 for routine follow-up and was found to have nausea, weakness, decreased oral intake, and a recent fall when her 'legs gave out' in the bathroom. She also had some abdominal pain and persistent diarrhea. She had been taking ondansetron and prochlorperazine for the nausea, but it did not help. The patient had a few episodes of yellow/green emesis without blood and denied blood in her stool. She denied fevers, chills, chest pain, and dyspnea. She was admitted on 30-May-2019 to rule out GI GvHD.

The patient was found to have GI graft-versu- host disease on 31-May-2019 by biopsy of the stomach and rectum. The findings were histologically low Grade. There was no viral cytopathic change and no active inflammation. The patient was treated with methylprednisone, budesonide, and beclomethasone. She received TPN and was advanced to a Grade I GvHD diet. She then showed no further indication of GvHD. The patient was discharged on 17-Jun-2019 at which point the GvHD symptoms had resolved.

The patient then presented to the ED on 23-Jul-2019 complaining of worsening generalized fatigue and weakness. On admission the patient's blood pressure was 90/60 which improved to 111/70 after one liter of intravenous (IV) fluid. The patient was initially suspected to have a UTI as a urinalysis showed 50-100 WBCs,

positive nitrates, and 4+ bacteria. The patient was started on ceftriaxone (Rocephin) but it was discontinued after urine culture grew 50-99K *E. coli* and a UTI was deemed unlikely. Blood culture on admission was found to be positive for oxacillin resistant *Staphylococcus epidermidis*. The patient was started on vancomycin to be continued until 31-Jul-2019. Cardiac imaging found a small abnormality on mitral valve of unclear significance. The patient was discharged on 03-Sep-2019.

The patient was seen in clinic on 04-Oct-2019 and was in her usual health. On the same day she tripped while walking and fell. She had bruises and abrasions on her arms. She did not lose consciousness or have any seizures. She had acute leg pain. X-ray found an acute, minimally displaced, transcervical left femoral neck fracture. Orthopedics was consulted and the decision was to transfer her for surgery. Of note, the patient had recently had a dual energy X-ray absoptiometry (DEXA) scan on 06-Sep-2019, with T scores of -2.0 on lumbar spine and -2.8 on femoral neck and was about to start alendronate in addition to vitamin D/calcium.

The patient was admitted on 06-Oct-2019 for left hip fracture. She had non-neutropenic fevers in the morning of 06-Oct-2019 and UTI was suspected given positive screen. Cefepime for *E. coli* UTI was started on 07-Oct-2019. The patient underwent a left hip hemiarthroplasty procedure on 08-Oct-2019. The patient was discharged on 15-Oct-2019 to a skilled nursing facility after resolution of the UTI. She was in stable condition. The plan was to continue deep vein thrombosis (DVT) prophylaxis for 6 weeks with enoxaparin 30 mg twice daily, weight bearing as tolerated, physical therapy, and hydromorphone as needed for pain.

The patient then presented to the ED on 17-Oct-2019 with fatigue, nausea, and diarrhea. On route to the ED, her HR was 127, BP was 134/92, and oxygen saturation was 95% on room air. In the ED, she underwent infectious workup with blood cultures, urinalysis, and chest X-ray that were unrevealing. She then underwent a CT scan which showed a right lower lobe subsegmental pulmonary embolism, with wedge-shaped consolidation suspicious for pulmonary infarct. The patient was admitted and started on enoxaparin 1 mg/kg q12hr. She was discharged in stable condition to a skilled nursing facility on 19-Oct-2019. The plan was to continue physical therapy.

On 14-Dec-2019 the patient was readmitted with positive staph bacteremia and was started on IV daptomycin. An echocardiogram found an abnormality on the anterior mitral valve, presumed to be endocarditis secondary to an infected MediPort. The MediPort was removed during the hospital course. The patient was kept on daptomycin for six weeks. On 14-Dec-2019 the patient was changed from prophylactic to therapeutic enoxaparin for 3-6 months. Repeat cultures done during the hospital stay remained negative. The patient was discharged on daptomycin with diagnosis of endocarditis secondary to staph bacteremia port infection.

On 08-May-2020, the patient was seen in clinic for a routine physical exam and was found to have significant dysphagia, causing significant weight loss and pill retention. She was admitted for IV fluids, IV medication, nutrition consult, and endoscopy. Endoscopy on 09-May-2020 showed esophageal erythema and gastritis/duodenitis. Schatzki's ring resolved with insufflation. Biopsy showed duodenal mucosa with gastric foveolar metaplasia, esophagitis with intraepithelial eosinophils, no evidence of colitis, and no evidence of GvHD. Sigmoidoscopy performed on 09-May-2020 showed normal colon and rectum. The patient received a swallow evaluation and was "cleared". She received omeprazole, mirtazapine, and a Dob Hoff tube. She was able to tolerate tube as well as oral feedings. The patient’s phosphorous dropped on 15-May-2019 to 0.9 but there was otherwise no evidence of refeeding syndrome. The patient was discharged on 16-May-2020 with a good appetite and calorie intake.

Subject Identifier	GP3OHS-002
Age	22
Sex	Male
Baseline Weight (kg)	71.8
Race	White – South or Central American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	30 Aug 2019
Event	Relapse of Disease

Severity	Grade 1
Serious (Yes/no)	Yes
Start/stop date of Event	27 Nov 2019 – 31 Aug 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3OHS-002 is a 22 year-old White, South or Central American, Hispanic or Latino, male with lymphoma who received an Unmanipulated CBU transplant on 30-Aug-2019.

The patient was diagnosed with stage IV lymphoma (Hodgkin lymphoma, classical mixed cellularity) on 06-Apr-2011. He received treatment with six cycles of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) from the time of diagnosis to Feb-2013, followed by three cycles of ABVD (Feb-2013 to Aug-2013), six cycles of brentuximab (30-Dec-2016 to 14-Apr-2017), three cycles of ifosfamide, carboplastin, and etoposide (ICE) from 13-May-2017 to 25-Jun-2017, 14 cycles of pembrolizumab (28-Jul-2017 to 05-Jun-2018), three cycles of gemcitabine, vinorelbine, and doxorubicin (GVD) from 25-Jun-2018 to 13-Aug-2018, three cycles of bendamustine (28-Nov-2018 to 29-Jan-2019), and radiation therapy (four fractions 04-Oct-2018; nine fractions 11-Oct-2018; one fraction 18-Oct-2018; five fractions 25-Oct-2018; one fraction 26-Oct-2018). The patient had moderate pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (26-Aug-2019 to 29-Aug-2019), fludarabine (22-Aug-2019 to 24-Aug-2019), and cyclophosphamide 4300 mg/day (22-Aug-2019 to 23-Aug-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, voriconazole, levofloxacin, posaconazole, pentamidine, and trimethoprim-sulfamethoxazole. Neutrophil counts recovered at 26 days post-transplantation (25-Sep-2019). The patient was discharged from the hospital on 25-Sep-2019.

Evaluation of the patient's disease status on 26-Sep-2019 demonstrated complete donor chimerism. Bone marrow showed no evidence of Hodgkin lymphoma. Cytogenetics and FISH analysis demonstrated 100% female donor cells. Then on 27-Nov-2019, the patient underwent a routine PET scan from skull to mid-thighs which showed evidence of disease progression with multiple new bilateral hypermetabolic nodes in cervical stations 2A and 2B/3. Multiple small abdominal mesenteric nodes with low level, moderate uptake, were also suspicious for new disease involvement. At that time there was no palpable adenopathy. The PI deemed the results of this PET scan as a confirmation of disease relapse on 27-Nov-2019. Platelet counts down trended slowly while other peripheral blood counts remained within normal limits. Due to probable early relapse of disease, a tacrolimus taper was initiated on 04-Jan-2020, with the patient off tacrolimus by 23-Jan-2020.

The patient was seen on 04-Mar-2020 for disease evaluation. A PET scan suggested disease progression (fluorodeoxyglucose avid lymphadenopathy in the mediastinum and neck; pulmonary findings suggestive of viral infection). The patient was sent for lymph node biopsy. Pathology was found to be reactive only, with no evidence of Hodgkin lymphoma. The plan was to repeat the biopsy as it was possible that the patient had reactive adenopathy due to a maturing immune system from the cord blood transplant. The patient was seen in clinic on 15-Apr-2020 and was noted to be clinically improving.

A follow-up PET scan was performed on 15-Jun-2020 which revealed multiple hypermetabolic lymph nodes consistent with residual lymphoma. The PET scan showed overall improvement since 02-Mar-2020, except for a right hilar lymph node which showed slightly increased uptake. The previously described bilateral hypermetabolic consolidative pulmonary opacities had resolved.

The patient had follow-up imaging done on 31-Aug-2020 which was read as a score of Deauville 3, consistent with remission. The investigator determined that since the patient experienced some cutaneous symptoms suggestive of chronic GvHD after immune suppression withdrawal, the previously seen inflammatory response may have been donor derived which provided a graft versus lymphoma effect. Therefore, based on the imaging results from 31-Aug-2020, the patient was deemed to be in remission and the disease relapse event was considered resolved.

Subject Identifier	GP3OHS-003
Age	46
Sex	Male
Baseline Weight (kg)	80.7
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	20 Sep 2019
Event	1. Acute GvHD 2. Multifocal Pneumonia 3. Enterobacter Bacteremia 4. Epistaxis 5. Pseudomonas Pneumonia
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3 5. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 23 Nov 2019 – 03 Jan 2020 2. 18 Dec 2019 – 03 Jan 2020 3. 16 Jan 2020 – 24 Jan 2020 4. 06 Feb 2020 – 10 Feb 2020 5. 11 Feb 2020 – 30 Mar 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Death
Relationship To The Study Drug	1. Yes 2. No 3. No 4. No 5. No
Date Of Death (If Applicable)	30 Mar 2020

Narrative:
Patient GP3OHS-003 is a 46 year-old White male with ALL who received a Omidubicel transplant on 20-Sep-2019.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor B-Cell ALL) on 05-Jan-2015. He underwent induction therapy with hyper-CVAD 1A with dasatinib and intrathecal chemotherapy (08-Jan-2015) and hyper-CVAD 1B with dasatinib and intrathecal chemotherapy (04-Feb-2015), consolidation therapy with hyper-CVAD 2A with dasatinib and intrathecal chemotherapy (27-Feb-2015) and hyper-CVAD 2B with dasatinib (20-Mar-2015), maintenance therapy with dasatinib (27-Feb-2015 to 08-Sep-2016), and reinduction therapy with nilotinib (03-Sep-2016 to 04-Mar-2018), 1 cycle of hyper-CVAD-B with Bosutinib and intrathecal chemotherapy (09-Mar-2018 to 22-Apr-2019), and three cycles of hyper-CVAD-B with Ponatinib and intrathecal chemotherapy (23-Apr-2019 to 17-Jul-2019). The patient's past medical history also included DVT of the upper extremity (26-Jul-2019). He had severe pulmonary (DLCO 62%) and moderate/severe hepatic impairment at study screening. Surgical history included left leg tibia and fibula fracture repair with skin flap (1991).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (16-Sep-2019 to 19-Sep-2019), fludarabine 55 mg/day (13-Sep-2019 to 15-Sep-2019), and cyclophosphamide 6000 mg/day (13-Sep-2019 to 14-Sep-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, fluconazole, trimethoprim-sulfamethoxazole, levofloxacin, and posaconazole. Neutrophil counts recovered at 13 days post-transplantation (03-Oct-2019). The patient was discharged from the hospital on 05-Nov-2019.

The patient was discharged from the transplant admission with mild to moderate diarrhea due to GI GvHD complicated by astrovirus infection. After discharge, the patient was consistently hypovolemic when assessed in clinic for scheduled outpatient evaluations. During these exams, it was noted that the patient had developed mild oral GvHD. Providers identified a need for TPN as diarrhea severity increased. The patient had clinically significant weight loss along with mild abdominal pain. There was no report of fevers.

On 23-Nov-2019, the patient required hospitalization for management of GvHD of the skin, mouth, and GI tract due to ongoing diarrhea and new oral GvHD. The patient's prednisone dose was increased from 10 mg twice a day to 40 mg twice a day with plan to taper every 5 days by 25%. TPN was continued through admission. The patient underwent flexible sigmoidoscopy on 25-Nov-2019, which was consistent with GI GvHD. The patient was started on Jakafi 5mg twice a day on 27-Nov-2019 for steroid-refractory GI GvHD. The patient's symptoms subsequently improved with this medication regimen and TPN was discontinued after meeting calorie goals. The patient was discharged home on 12-Dec-2019 with continued follow-up care in the outpatient setting.

The patient was then admitted for multifocal pneumonia and staph bacteremia from 18-Dec-2019 to 03-Jan-2020. During the admission, the patient was noted to have significantly improved stool output. The provider deemed the patient clinically stable regarding his GvHD and the acute GvHD event was considered resolved with no residual effects on 03-Jan-2020. The patient was then admitted for Enterobacter bacteremia from 16-Jan-2020 to 24-Jan-2020. He was adequately treated with cefepime and discharged on ciprofloxacin. The patient was discharged to a skilled nursing facility but was readmitted from 06-Feb-2020 to 10-Feb-2020 for epistaxis that required multiple platelet transfusions.

During transport back to the skilled nursing facility on 10-Feb-2020, the patient experienced a worsening productive cough with a new oxygen requirement. The patient had associated shortness of breath and dyspnea on exertion, but denied fevers, chills, or night sweats. He had some high-pitched breath sounds but denied increased work of breathing. The patient was taken to the emergency room on 11-Feb-2020 and was placed on 4 liters of oxygen via nasal canula. The patient was admitted and was noted to have a respiratory rate of 29 with tracheal stenosis so he was placed on intermittent BiPAP. Acid-fast bacilli test and blood cultures were done. Flu A/B and respiratory syncytial virus (RSV) were negative.

CT of the chest showed no pulmonary embolism. It did show marked tracheal narrowing, new thickening of the trachea with surrounding inflammation, and fat stranding which was suspicious for an infectious process. There was extensive debris in the airways, complete occlusion of the left lower lobe, and tree-in-bud nodularity within the right lower lobe, all suggestive of aspiration/aspiration pneumonia. Chest X-ray showed new left lower lobe patchy ground-glass opacity suggestive of pneumonia. The patient was started on vancomycin, azithromycin, micafungin, and cefepime.

On 12-Feb-2020, the patient required intubation. A bronchoalveolar lavage was done on 12-Feb-2020 which did not reveal thick secretions. Cultures were obtained and were positive for Pseudomonas aeruginosa. The patient was given dexamethasone 10 mg and started on dexamethasone 4 mg every 6 hours. Antibiotic coverage included ceftolozane-tazobactam 3 grams intravenous (IV) every 8 hours and tobramycin 5mg/kg IV every 24 hours. The patient improved and was extubated on 15-Feb-2020 to a nasal cannula. Antibiotics were narrowed to cefepime based upon culture sensitivities. Peripherally inserted central catheter line was removed, and once cultures cleared, and a new PICC line was placed. The patient continued to improve and was discharged on 24-Feb-2020 continuing cefepime 2 grams IV every 8 hours.

The patient then visited an outside ED on 12-Mar-2020 for dyspnea and anemia. He was treated with two units of packed RBC. The patient was cleared for discharge after showing improvement but required admission on 13-Mar-2020 for pneumonia of both lungs. The patient was found to have positive Pseudomonas and Enterobacter cultures. On 21-Mar-2020, the patient was transferred to the transplant center and was intubated with severe ARDS presumed to be due to pneumonia. His clinical condition continued to decline while intubated and the patient died on 30-Mar-2020. Primary cause of death was noted as bacterial infection and secondary cause as acute respiratory failure/ARDS due to pneumonia. Autopsy was not done.

Subject Identifier	GP3OHS-004
Age	54
Sex	Female
Baseline Weight (kg)	67.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	25 Oct 2019
Event	Inflammatory Colitis
Severity	Grade 2
Serious (Yes/no)	Yes
Start/stop date of Event	09 Jan 2020 – 14 Jan 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	Yes
Date Of Death (If Applicable)	

Narrative:
Patient GP3OHS-004 is a 54-year-old White female with Myelodysplastic Syndrome who received an Unmanipulated CBU transplant on 25-Oct-2019.

The patient was diagnosed with Myelodysplastic Syndrome (refractory anemia with excess blasts in transformation, RAEB-2) on 10-May-2019. She underwent induction therapy with three cycles of azacitidine (28-Jun-2019 to 19-Jul-2019). The patient's past medical history included fibroids, DVT of the bilateral upper extremities, and depression. She had moderate pulmonary impairment at study screening. She had reported allergies to sulfonamide antibiotics and cefepime.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 150 cGy/day (21-Oct-2019 to 24-Oct-2019), fludarabine 43 mg/day (18-Oct-2019 to 20-Oct-2019), and cyclophosphamide 3000 mg/day (18-Oct-2019 to 19-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included valacyclovir, posaconazole, levofloxacin, and pentamidine. Neutrophil counts recovered at 24 days post-transplantation (18-Nov-2019). The patient was discharged from the hospital on 20-Nov-2019.

On 09-Jan-2020, the patient presented to the emergency room with abdominal pain. The abdominal pain had started two weeks prior (25-Dec-2019) and had progressively worsened. The pain was in the bilateral lower quadrants, was reported as cramping in quality, and worsened with food intake. The patient rated the pain as 8/10. She also reported decreased appetite and daily episodes of diarrhea. The patient was treating the diarrhea with loperamide hydrochloride without significant effect.

A CT scan of the abdomen and pelvis performed in the emergency room showed diffuse colitis. The patient was admitted for evaluation of GvHD. Infectious stool studies were negative. On 13-Jan-2020, an esophagogastroduodenoscopy and flexible sigmoidoscopy was performed. Biopsies obtained were negative for GvHD and favored the diagnosis of cord colitis. The patient began treatment with ciprofloxacin and metronidazole for cord colitis. She was discharged on 14-Jan-2020 at which point the inflammatory colitis event was considered resolved.

Subject Identifier	GP3OHS-005
Age	56
Sex	Female
Baseline Weight (kg)	57.2
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	15 Nov 2019
Event	Gastritis
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	13 Jan 2020 – 16 Jan 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3OHS-005 is a 56-year-old White female with AML who received a Omidubicel transplant on 15-Nov-2019.

The patient was diagnosed with AML on 02-May-2019. She underwent induction therapy with one cycle of cytarabine and idarubicin (24-May-2019 to 30-May-2019), consolidation therapy with two cycles of azacitidine (23-Sep-2019 to 27-Sep-2019), and reinduction therapy with one cycle of FLAG and idarubicin (28-Jun-2019 to 02-Jul-2019). The patient's past medical history included migraines, Type II diabetes, psychiatric disturbance (depression or anxiety requiring psychiatric consult or treatment), and elevated liver function test (LFTs). Surgical history included an appendectomy in 1974. She had reported allergies to prochlorperazine and pneumococcal vaccine.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (11-Nov-2019 to 14-Nov-2019), fludarabine (08-Nov-2019 to 10-Nov-2019), and cyclophosphamide (08-Nov-2019 to 09-Nov-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included voriconazole, pentamidine, posaconazole, acyclovir, trimethoprim-sulfamethoxazole, and levofloxacin. Neutrophil counts recovered at 19 days post-transplantation (03-Dec-2019). The patient was discharged from the hospital on 03-Dec-2019.

The patient was admitted on 13-Jan-2020 for non-neutropenic fevers after an esophagogastroduodenoscopy and flexible sigmoidoscopy that was performed for suspected GvHD. She reported issues with persistent nausea, poor appetite, and weight loss over the previous couple of weeks. Beclomethasone had been started with only minor improvement in symptoms, so she had been referred for scoping. The evening after the procedure, the patient developed fevers up to 101.4°F at home. She reported feeling chilled at the time but denied rigors. She vomited once on the way to the emergency department (ED). She denied having abdominal pain, diarrhea, or melena.

In the ED blood cultures were drawn and a chest X-ray was obtained which was clear. Antibiotics were not administered, and the patient returned home. The following day she awoke with fevers up to 101.6°F. She had nausea at home which was managed with ondansetron and olanzapine. She presented to the clinic and was given a dose of piperacillin-tazobactam. She was admitted for further workup and management of her fevers.

Mycophenolate mofetil was stopped on 14-Jan-2020 (post-transplantation Day +60) per protocol. The patient was discharged on 16-Jan-2020 with the diagnosis of gastritis after the patient's nausea had significantly improved. Biopsies from the endoscopy on 13-Jan were inconclusive, so the decision was made to continue monitoring rather than starting steroids.

Subject Identifier	GP3OHS-006
Age	66
Sex	Male
Baseline Weight (kg)	107.5
Race	White
Study Therapy	N/A
Date Of Study Therapy Administration	N/A
Event	No SAEs Reported
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	

Narrative:
Patient GP3OHS-006 is a 66 year-old White male with ALL who did not receive a study transplant within 90 days of randomization. The patient's BM was deemed to be too necrotic, with remaining disease involvement requiring additional treatment per the investigator.

The patient was diagnosed with ALL on 03-Oct-2019. He underwent induction therapy with one cycle of hyper-CVAD (01-Nov-2019 to 08-Nov-2019). Consolidation therapy included one cycle of methotrexate (01-Nov-2019) and maintenance therapy included dasatinib (01-Oct-2019 to 14-Oct-2019 and 21-Oct-2019 to 20-Nov-2019) and one cycle of blinatumomab (21-Jan-2020 to 18-Feb-2020). The patient's past medical history included prostate cancer. He had moderate pulmonary impairment at study screening (DLCO = 73%). Surgical history included prostatectomy (2016), shoulder surgery (2011), appendectomy (1958), and fusion of a finger. He had reported allergies to trimethoprim-sulfamethoxazole.

The patient received a cord blood SCT on 10-Jul-2020 and was reported to still be alive at the month 15 study-related visit on 09-Apr-2021. His disease was in remission on that date.

Subject identifier	GP3PMC-001
Age	16
Sex	Male
Baseline weight (kg)	77.4
Race	White – European
Study therapy	Unmanipulated CBU
Date of study therapy administration	07 Dec 2018
Event	1. Disease Relapse 2. Line Infection
Severity	1. Grade 4 2. Grade 3
Serious (yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 12 Nov 2019 – 07 Dec 2019 2. 12 Nov 2018 – 20 Nov 2018
Outcome of event	1. Resolved by convention 2. Resolved
Relationship to the study drug	1. No 2. NA: Pre-transplant event
Date of death (if applicable)	

Narrative:
Participant GP3PMC-001 is a 16-year-old White, European male with Acute Myelogenous Leukemia who received an unmanipulated cord blood unit transplant on 07-Dec-2018.

The participant was diagnosed with Acute Myelogenous Leukemia (minimally differentiated AML - M0), with CNS involvement, on 16-Jan-2017. He underwent two cycles of induction therapy according to the NOPHO-DBH AML 2012 protocol. First induction course included mitoxantrone, etoposide, and cytarabine (19-Jan-2017), and the second induction course included cytarabine, etoposide, and daunorubicin (03-Jan-2017). Three cycles of consolidation therapy according to the NOPHO-DBH AML 2012 protocol were given (dates unknown). Reinduction therapy included a cycle of FLAG with daunorubicin (25-Sep-2018) and a cycle with FLAG only. The participant's past medical history included parainfluenza pneumonia (Oct-2018), *E. coli* sepsis (Oct-2018), and central line infection (Nov-2018). He had reported allergies to vancomycin and amphotericin B.

Prior to unmanipulated cord blood unit transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine 99 mg/day (02-Dec-2018 to 04-Dec-2018), thiotepa 390 mg/day (30-Nov-2018 to 01-Dec-2018), and busulfan 242 - 395 mg/day (02-Dec-2018 to 04-Dec-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included voriconazole, valacyclovir, acyclovir, and ciprofloxacin. Neutrophil counts recovered at 17 days post-transplantation (24-Dec-2018). The participant was discharged from the hospital on 28-Dec-2018.

On 12-Nov-2019, the participant was admitted to the hospital with painful skin lesions. Cytomorphology of peripheral blood leukocytes showed 88% blasts and the participant was diagnosed with relapsed AML on 12-Nov-2019. On 13-Nov-2019, the participant underwent a bone marrow aspiration which showed >5% leukemic blasts. On the same date, a lumbar puncture was performed, and the cerebrospinal fluid was positive for leukemic cells. The participant elected to start gemtuzumab (Mylotarg) monotherapy on 14-Nov-2019. The treatment course was complicated by febrile neutropenia and painful skin lesions on 15-Nov-2019.

The participant was diagnosed with refractory AML with 67% blast by cytomorphology on 21-Nov-2019 (day +349). He was started on clofarabine/cytarabine on 22-Nov-2019. The participant's treatment course was complicated by circular insufficiency and sepsis on 03-Dec-2019. Blood cultures were positive for *Candida* on 05-Dec-2019 and treatment was initiated with fluconazole. On 07-Dec-2019, blood cultures were positive for *Micrococcus luteus*. On 09-Dec-2019, cytomorphology showed 0% blasts.

During the LTF study, blasts reappeared in the participant's peripheral blood on 26-Feb-2021 confirming relapsed disease (day +812). Palliative care was initiated with venetoclax on 29-Mar-2021. Relapse was determined to be the primary cause of death on 10-Apr-2021. An autopsy was not performed.

Subject Identifier	GP3PMC-002
Age	18
Sex	Male
Baseline Weight (kg)	59.0
Race	White - European
Study Therapy	Omidubicel
Date Of Study Therapy Administration	03 May 2019
Event	1. BK Cystitis 2. Renal Failure 3. Sinopulmonal Aspergillus Infection
Severity	1. Grade 3 2. Grade 3 3. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 24 May 2019 – 21 Jun 2019 2. 29 May 2019 – 09 Jun 2019 3. 21 Mar 2019 – 12 Apr 2019

Outcome Of Event	1. Resolved with sequelae 2. Resolved 3. Resolved
Relationship To The Study Drug	1. No 2. No 3. NA: Pre-transplant Event
Date Of Death (If Applicable)	

Narrative:
Patient GP3PMC-002 is an 18 year-old White, European male with AML who received a Omidubicel transplant on 03-May-2019.

The patient was diagnosed with AML on 16-Jul-2016. He underwent induction and consolidation therapy with NOPHO-DBH AML 2012 protocol (course 1 mitoxantrone, etoposide, and cytarabine (MEC) 16-Jul-2016; course 2 FLADx 30-Aug-2016; course 3 HAM:L 25-Oct-2016; course 4 HA3E 13-Dec-2016; course 5 FLA 24-Jan-2017). Reinduction therapy cycle 1 included fludarabine, daunorubicin, and cytarabine (10-Feb-2019 to 14-Feb-2019) and reinduction cycle 2 included fludarabine and cytarabine (16-Mar-2019 to 20-Mar-2019). The patient's medical history included cardiac impairment (EF = 49% on 20-Mar-2019) and Staphylococcus hominis sepsis (11-Feb-2019). The patient had a sinopulmonal Aspergillus infection at study screening. His surgical history included functional endoscopic sinus surgery and infundibulotomy (21-Mar-2019).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (28-Apr-2019 to 30-Apr-2019), thiotepa (26-Apr-2019 to 27-Apr-2019), and busulfan (28-Apr-2019 to 30-Apr-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included amphotericin B, ciprofloxacin, and acyclovir. Neutrophil counts recovered at seven days post-transplantation (10-May-2019). The patient was discharged from the hospital on 21-Jun-2019.

On 23-May-2019, the patient was found to be urine culture positive for BK cystitis. Symptomatic treatment for BK cystitis included IV hyperhydration, pain medication, and oxybutynin. The patient was dependent on TPN and his hospitalization was prolonged due to suboptimal food intake in part due to altered taste and the patient refusing tube feeds. On 29-May-2019, the patient was found to have elevated creatinine and potassium (6.5 mmol/L) indicative of renal failure. Suspected causes included drug toxicities or infection (BK cystitis). Mycophenolate mofetil, cyclosporine, and isavuconazole were therefore stopped. Abdominal echo on 29-May-2019 showed increased bladder thickness corresponding with cystitis. Echocardiography on 29-May-2019 showed no evidence of pericarditis. Blood culture CMV and HHV6 returned positive on 03-Jun-2019.

On 09-Jun-2019, kidney echo demonstrated hemorrhagic cystitis with no clots visible in the kidneys but with the bladder composed of 50% clots (max diameter 5.4 cm) and no urinary tract obstruction. The patient's creatinine and potassium stabilized, and the renal failure event was considered resolved on 09-Jun-2019. On 15-Jun-2019 the patient was still persistently febrile and required hyperhydration. The patient was discharged on 21-Jun-2019. At the time micturition was still painful with hematuria.

Subject Identifier	GP3PMC-003
Age	14
Sex	Male
Baseline Weight (kg)	67.6
Race	White – European
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	07 Nov 2019
Event	1. PGF 2. *S. mitis* Infection
Severity	1. Grade 4 2. Grade 1
Serious (Yes/no)	1. Yes 2. Yes

Start/stop date of Event	1. 29 Nov 2019 – 29 Dec 2019 2. 07 Oct 2019 – 19 Oct 2019
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. Yes 2. NA: Pre-transplant event
Date Of Death (If Applicable)	

Narrative:
Patient GP3PMC-003 is a 14 year-old White, European male with AML who received an Unmanipulated CBU transplant on 07-Nov-2019.

The patient was diagnosed with AML (without maturation - M1) on 23-Mar-2018. He underwent induction therapy with NOPHO-DBH AML 2012 protocol. This included course 1 with MEC (mitoxantrone, cytarabine, and etoposide; 28-Mar-2018), course 2 with ADE (cytarabine, daunorubicin, and etoposide), course 3 with HAM (cytarabine and mitoxantrone; 13-Jun-2018), course 4 with HA3E (cytarabine and etoposide; 18-Jul-2018), and course 5 with FLA (fludarabine and cytarabine; 15-Aug-2018). He received reinduction therapy with FLA-DNR on 23-Aug-2019. The patient's past medical history included suspected pulmonary aspergillosis on CT thorax (04-Aug-2018), suspected cerebral lesions from aspergillosis or toxoplasmosis on brain MRI (17-Aug-2018), and a severe pulmonary impairment at study screening (cDLCO = 64% on 19-Sep-2019). He had reported allergies to vancomycin, teicoplanin, and thrombocytes.

Prior to starting the conditioning regimen, the patient developed a fever during a blood transfusion and was admitted on 07-Oct-2019. He was discharged the following day but developed a fever of 39.4°C at home and was readmitted. Blood cultures drawn on 09-Oct-2019 were positive for *Streptococcus mitis*. He received intravenous antibiotic therapy with daptomycin through discharge on 19-Oct-2019.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 90 mg/day (02-Nov-2019 to 04-Nov-2019), thiotepa 350 mg/day (31-Oct-2019 to 01-Nov-2019), and busulfan 242 - 300 mg/day (02-Nov-2019 to 04-Nov-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included amphotericin B, ciprofloxacin, and acyclovir.

Post-transplantation laboratory results indicated suspected engraftment failure as no leukocytes were detected in blood samples. Filgrastim was increased to 10 µg/kg on 25-Nov-2019 with no effect. On 29-Nov-2019 (post-transplantation Day +22), BM aspirate showed no leukocytes (aplastic marrow) leading to the diagnosis of PGF. Reduction of immunosuppression was initiated on 29-Nov-2019. Mycophenolate mofetil was stopped and cyclosporine dose was reduced. The patient then went on to receive an additional SCT (donor Type unknown) on 13-Dec-2019. Neutrophil engraftment was confirmed on 29-Dec-2019.

Subject Identifier	GP3PMC-004
Age	14
Sex	Male
Baseline Weight (Kg)	51.7
Race	Black – African
Study Therapy	Omidubicel
Date Of Study Therapy Administration	11 Feb 2020
Event	1. Hepatic Veno-Occlusive Disease 2. Renal Function Disorder 3. VZV Reactivation 4. Fever with Circular Insufficiency 5. *S. mitis* Infection
Severity	1. Grade 3 2. Grade 2 3. Grade 3

	4. Grade 3 5. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 12 Feb 2020 – 04 Mar 2020 2. 30 Mar 2020 – 06 Apr 2020 3. 19 Aug 2020 – 22 Aug 2020 4. 11 Dec 2019 – 11 Mar 2020 5. 10 Nov 2019 – 22 Nov 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved with sequelae 4. Resolved 5. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. NA: Pre-transplant event 5. NA: Pre-transplant event
Date Of Death (If Applicable)	

Narrative:
Patient GP3PMC-004 is a 14 year-old Black, African (both parents born in Africa) male with AML who received a Omidubicel transplant on 11-Feb-2020.

The patient was diagnosed with AML on 09-Sep-2019. He underwent induction therapy with NOPHO-AML protocol. This included course 1 with MEC (mitoxantrone, cytarabine, and etoposide; 10-Sep-2019 to 22-Sep-2019), course 2 with ADE; 25-Oct-2019 to 02-Nov-2019), and course 3 with HAM (cytarabine and mitoxantrone; 29-Nov-2019 to 03-Dec-2019). Consolidation therapy included clofarabine/Ara-c (31-Dec-2019) and gemtuzumab ozogamicin (09-Jan-2020). The patient's past medical history included suspected adrenal cortex insufficiency since 05-Feb-2020 and colonization with *Citrobacter* (treated with meropenem). The patient was hospitalized with *Streptococcal mites* infection treated with vancomycin and meropenem from 10-Nov-2019 to 22-Nov-2019. He remained hospitalized and was treated for fever with cardiovascular insufficiency from 12-Dec-2019 to 11-Mar-2020. The patient had severe pulmonary impairment at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (06-Feb-2020 to 08-Feb-2020), thiotepa (04-Feb-2020 to 05-Feb-2002), and busulfan (06-Feb-2020 to 08-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included micafungin, vancomycin, and acyclovir. Neutrophil counts recovered at 10 days post-transplantation (21-Feb-2020). The patient was discharged from the hospital on 11-Mar-2020.

The patient was noted to have edema with a weight gain greater than 7% and a rise in liver enzymes on 12-Feb-2020, when he was admitted during the transplantation phase. Renal and pulmonary systems remained stable. A clinical diagnosis of hepatic veno-occlusive disease (VOD) was made. The patient was treated with furosemide for the edema and defibrotide for the VOD. The patient remained stable during treatment. The hepatic VOD event was resolved with no residual side effects on 04-Mar-2020 when the patient's liver enzymes stabilized.

The patient was then hospitalized on 30-Mar-2020 with complaints of vomiting, poor food intake, painful micturition, and hematuria. The patient had known BK cystitis at the time. The BK cystitis was treated with hyperhydration. The patient was found to have elevated potassium and creatinine. His symptoms and electrolyte levels were attributed to suspected renal function disorder due to possible underlying BK nephritis or cyclosporine/ganciclovir toxicity.

On 31-Mar-2020, the patient was found to have sinus tachycardia, pre-excitation, and/or intermittent left bundle branch block on electrocardiogram (ECG). The arrhythmia was likely caused by hyperkalemia. Holter monitoring resulted in prolonged hospitalization. The patient's renal function recovered on 06-Apr-2020 after hydration, cessation of vomiting, and lowered cyclosporine levels. The patient was found to have Wolf Parkinson White Syndrome on 07-Apr-2020.

The patient developed right foot dermatoses on 17-Aug-2020. Suspected VZV reactivation was treated with valacyclovir on 17-Aug-2020. The patient was then admitted on 19-Aug-2020 with symptoms of nausea, fever (38.5°C), and leg pain. The patient was treated with intravenous (IV) acyclovir and meropenem. There was a complication of Grade 3 extravasation with the IV acyclovir. Blood culture results were negative for bacteria and positive for VZV on 22-Aug-2020. The patient was discharged home on 22-Aug-2020.

Subject Identifier	GP3RAB-001
Age	21
Sex	Male
Baseline Weight (kg)	62.0
Race	White - Mediterranean
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	06 Jan 2020
Event	1. Severe GI Bleeding 2. GI GvHD 3. Septic Shock Due to Candida
Severity	1. Grade 4 2. Grade 3 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 04 Feb 2020 – 08 Feb 2020 2. 04 Feb 2020 – 20 Apr 2020 3. 15 Apr 2020 – 20 Apr 2020
Outcome Of Event	1. Resolved 2. Death 3. Death
Relationship To The Study Drug	1. Yes 2. Yes 3. No
Date Of Death (If Applicable)	20 Apr 2020

Narrative:
Patient GP3RAB-001 is a 21 year-old White, Mediterranean male with ALL who received an Unmanipulated CBU transplant on 06-Jan-2020.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor T-cell ALL) on 05-Sep-2019. He underwent induction therapy with cyclophosphamide 330 mg (05-Sep-2019 to 07-Sep-2019), daunorubicin 75 mg and vincristine 2 mg (08-Sep-2019), daunorubicin 75 mg (09-Sep-2019), daunorubicin 75 mg and vincristine 2 mg (15-Sep-2019), daunorubicin 75 mg (16-Sep-2019), and PEG-asparaginase 3300 u and vincristine 2 mg (06-Oct-2019). Consolidation therapy included methotrexate 2600 mg and vincristine 2 mg (27-Nov-2019), etoposide 430 mg (30-Nov-2019), and etoposide 430 mg and methotrexate 3500 mg (01-Dec-2019). The patient's past medical history included low ejection fraction and moderate pulmonary impairment. During induction therapy, the patient developed septic shock due to *Pseudomonas*. CMV was detectable prior to study transplant (12-Dec-2019).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 90 mg/day (01-Jan-2020 to 03-Jan-2020), thiotepa 315 mg/day (30-Dec-2019 to 31-Dec-2019), and busulfan 200 mg/day (01-Jan-2020 to 03-Jan-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included fluconazole, acyclovir, and ciprofloxacin. Ganciclovir was given for CMV reactivations. Neutrophil counts recovered at 14 days post-transplantation (20-Jan-2020).

Post-transplantation the patient suffered from recurrent neutropenic fevers with coagulase-negative Staphylococci bacteremia, severe oropharyngeal mucositis, and skin GvHD. The patient started experiencing diarrhea twice a day on 19-Jan-2020 accompanied by a small, microscopic rash on the back. Treatment with methylprednisolone 40 mg/day and cannabidiol was initiated. The patient's symptoms continued to worsen over the course of a week with the skin rash noted to be <25% of the body surface. Cyclosporine was stopped on 25-Jan-2020. Bilirubin then increased to 4.63 mg/dl. Cyclosporine was then restarted on 27-Jan-2020 and methylprednisolone was reduced. The patient had multiple systemic infections throughout his post-transplantation course including bacteremia/sepsis with *E. coli* (04-Feb-2020), pneumonia, and CMV reactivations.

On 04-Feb-2020, the patient had severe gastrointestinal bleeding with associated anemia (hemoglobin dropped to 5.0 mg/dl). The patient was therefore transferred from the bone marrow transplant (BMT) department to the ICU for a gastroscopy procedure and treatment. Cyclosporine was discontinued and methylprednisolone was continued at 100 mg/day. Biopsy results diagnosed gastrointestinal GvHD. The source of bleeding was not observable during the initial gastrostomy procedure and the bleeding continued. The patient underwent a second gastrostomy the following day. Blood clots were observed in the duodenum, so a gastrointestinal intervention was not possible. The patient was treated with supportive care including blood products and a proton-pump inhibitor with a plan to do an angiography if the bleeding exacerbated.

The patient was transferred back to the BMT unit on 08-Feb-2020. The patient's diarrhea worsened (x 5/day) and his bilirubin continued to increase (5.0-6.0 mg/dl). A one-time dose of cyclosporine was given on 09-Feb-2020 and then all calcineurin inhibitors were discontinued. Tacrolimus 1 mg/bid was started on 24-Feb-2020. Diarrhea and bilirubin continued to worsen in addition to an increase in creatine leading to acute kidney failure. Tacrolimus was stopped on 10-Mar-2020. The diarrhea and bilirubin continued to worsen, and the patient was treated with methylprednisolone 2 mg/kg/day. The patient had confirmed Grade IV GvHD with skin, liver, and GI involvement.

The hospital course was further complicated by cyclosporin-induced microangiopathy. On 15-Apr-2020, blood cultures revealed candidemia which led to septic shock. The GvHD continued to worsen and the bilirubin did not improve (8.0 - 12.00 mg/dl). The septic shock event was resolved by death on 20-Apr-2020. The primary cause of death was noted as fungal infection and secondary cause of death was noted as acute GvHD. Autopsy was not done.

Subject Identifier	GP3RCI-001
Age	49
Sex	Female
Baseline Weight (kg)	68.1
Race	Black, African American
Study Therapy	Not received
Date Of Study Therapy Administration	N/A
Event	1. Hypercalcemia 2. Progressive Disease
Severity	1. Grade 4 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 28 Dec 2019 – 03 Jan 2020

	2. 30 Dec 2019 – 20 Feb 2020
Outcome Of Event	1. Resolved 2. Death
Relationship To The Study Drug	1. NA: Pre-transplant event 2. NA: Pre-transplant event
Date Of Death (If Applicable)	20 Feb 2020
Narrative: Patient GP3RCI-001 is a 49 year-old Black, African American female with Human T-cell Leukemia/Lymphotropic Virus Type-1 (HTLV-1) associated adult T-cell leukemia/lymphoma who consented to participate in the Omidubicel GP3 study on 27-Nov-2019. The patient did not receive the study transplant. The patient was diagnosed with HTLV-related adult T-cell leukemia (ATLL) on 30-May-2019. She underwent therapy with etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin from 09-Jun-2019 to 12-Nov-2019 for a total of seven cycles. Her past medical history included a psychiatric disorder (anxiety or depression) and severe pulmonary impairment (cDLCO = 59%). Surgical history included fibroid removal. No drug allergies were reported at screening. Prior to starting the conditioning regiment for the transplant, the patient presented to the emergency department on 28-Dec-2019 with complaints of weakness, fatigue, and poor intake. Labs were significant for a calcium level of 15.8 mg/dL. The patient was diagnosed with hypercalcemia secondary to ATLL and admitted for treatment with intravenous fluids, zoledronic acid, and calcitonin. Calcium levels declined over the course of admission and achieved a normal level of 8.9 mg/dL on 03-Jan-2020. Upon admission, the patient was noted to have worsening right cranial nerve IV and VII palsies. A previously obtained MRI of the brain (09-Dec-2019) was concerning for leukemic infiltrate. A BM biopsy was performed on 30-Dec-2019 and confirmed disease relapse with mildly hypercellular marrow with maturing trilineage hematopoiesis and 15-25% involvement by aberrant CD4 positive T-cells compatible with adult T-cell leukemia/lymphoma. Peripheral blood results indicated moderate normocytic anemia with circulating abnormal lymphocytes. The patient was started on arsenic trioxide, interferon alpha, and zidovudine on 04-Jan-2020. After beginning the first cycle of treatment, the patient experienced acute kidney injury, severe lactic acidosis, and acute liver dysfunction possibly secondary to zidovudine or liver involvement of ATLL. On 15-Jan-2020, chemotherapy was held due to multi-organ failure. The patient continued to decline and enrolled in hospice on 19-Feb-2020. The patient passed away on 20-Feb-2020. Primary cause of death was noted as disease relapse. An autopsy was not performed.	

Subject Identifier	GP3RMH-001
Age	19
Sex	Male
Baseline Weight (kg)	74.0
Race	White – European
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	08 Nov 2019
Event	1. Infusion-Related Reaction – Platelets 2. PGF
Severity	1. Grade 2 2. Grade 4
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 27 Oct 2019 – 28 Oct 2019 2. 20 Dec 2019 – 02 Jan 2020
Outcome Of Event	1. Resolved 2. Resolved

Relationship To The Study Drug	1. No 2. Yes
Date Of Death (If Applicable)	

Narrative:
Patient GP3RMH-001 is a 19 year-old White, European male with Myelodysplastic Syndrome who received an Unmanipulated CBU transplant on 08-Nov-2019.

The patient was initially diagnosed with Hodgkin's lymphoma in March 2016. Therapy with cyclophosphamide, vincristine, and prednisolone was started on 17-Mar-2019. He received two cycles of cyclophosphamide, vincristine, prednisone, and doxorubicin (OEPA) which started on 22-Mar-2016 and 18-Apr-2016. He also received four cycles of cyclophosphamide, vincristine, prednisone, and dacarbazine (COPDAC) from 26-Mar-2016 through 30-Aug-2016. Myelodysplastic Syndrome – refractory cytopenia with multilineage dysplasia (RCMD) – was diagnosed on 02-Jul-2019. The patient's past medical history included asthma. He had moderate pulmonary impairment at study screening.

Before admission to begin the conditioning regimen, the patient received a platelet transfusion on 27-Oct-2019 during which he developed a generalized rash. He was admitted for observation and discharged the following day after the rash had resolved. A platelet antibody screen drawn at the time of the reaction was negative.

Prior to the Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 50 mg/day (01-Nov-2019 to 03-Nov-2019), cyclophosphamide 4720 mg/day (02-Nov-2019 to 03-Nov-2019), and TBI 165 cGy (04-Nov-2019 to 07-Nov-2019). GvHD prophylaxis included mycophenolate mofetil (MMF) and cyclosporine. Infection prophylaxis included ciprofloxacin, acyclovir, letermovir, posaconazole, penicillin, and diaminodiphenyl sulfone (Dapsone). A deviation was recorded for the G-CSF treatment of the patient. G-CSF was erroneously held between post-transplant days 7 and 17.

On 09-Dec-2019 (post-transplant Day +35), post-transplant chimerisms by BM aspirate showed 87% donor cells; however, WBC counts resulted as 0.10 x 10^{9th}. The BM biopsy revealed marked hypocellularity (5-7%). The pathologist commented that if the sample was representative of the BM, it would indicate poor/delayed engraftment, but as noted the degree of cellularity could be an underestimate. On 20-Dec-2019 (post-transplant Day +42), WBC counts remained at 0.10 x 10^{9th}. The patient did not achieve an ANC greater or equal to 0.5 x 10^9^{th}/L for three consecutive measurements on different days. Therefore, the patient met criteria for PGF on post-transplant Day +42 per protocol definition.

The PGF event was reported as resolved on 02-Jan-2020 which was the date of neutrophil engraftment (post-transplant Day +55). There was no treatment given for the graft failure.

Subject Identifier	GP3SCI-003
Age	54
Sex	Female
Baseline Weight (kg)	60.8
Race	Black – African American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	03 May 2019
Event	1. Acute GvHD 2. Diarrhea 3. Relapse 4. Multi-organ Failure
Severity	1. Grade 3 2. Grade 3 3. Grade 5 4. Grade 4
Serious (Yes/no)	1. Yes 2. Yes

	3. Yes 4. Yes
Start/stop date of Event	1. 27 May 2019 – 19 Sep 2019 2. 09 Sep 2019 - 19 Sep 2019 3. 06 Sep 2019 -19 Sep 2019 4. 16 Sep 2019 - 19 Sep 2019
Outcome Of Event	1. Death 2. Death 3. Death 4. Death
Relationship To The Study Drug	1. Yes 2. No 3. No 4. No
Date Of Death (If Applicable)	19 Sep 2019

Narrative:
Patient GP3SCI-003 is a 54 year-old Black, African American female with acute myeloid leukemia who received an Unmanipulated CBU transplant on 03-May-2019.

The patient was diagnosed with Acute Myeloid Leukemia on 21-Jan-2019. She underwent treatment with induction 7+3 and midostaurin and consolidation with one cycle of HiDAC and midostaurin. She was found to be in remission with MRD on BM biopsy on 12-Apr-2019. The patient's past medical history included hypertension, adnexal fibroids, and hyperlipidemia. She had a history of *Clostridium difficile* infection following induction therapy. She had moderate pulmonary impairment at study screening (cDLCO = 75%).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (29-Apr-2019 to 02-May-2019), fludarabine 45 mg/day (26-Apr-2019 to 28-Apr-2019), and cyclophosphamide 4320 mg/day (26-Apr-2019 to 27-Apr-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included fluconazole, acyclovir, and levofloxacin. Neutrophil counts recovered at 16 days post-transplantation (19-May-2019). The patient was discharged from the hospital on 23-May-2019.

The patient was noted to have an erythematous rash with engraftment. The rash resolved with solumedrol 60 mg on 18-May-2019. The patient also reported persistent nausea and vomiting throughout her transplant admission which persisted upon discharge. The patient then developed progressive diarrhea (10 episodes/day) and had reappearance of her diffuse, pruritic skin rash on 26-May-2019. She was then admitted on 27-May-2019 for further workup and evaluation of acute GvHD vs. infection. On admission blood cultures were drawn, GI PCR and *C. difficile* labs were ordered, and the patient received two 1 L normal saline boluses.

Esophagogastroduodenoscopy, flexible sigmoidoscopy, and skin biopsy were completed on 28-May-2019. Pathology reports were consistent with GvHD of the GI tract. Immunohistochemical stains for CMV and adenovirus were negative. Skin biopsy was reported as interface dermatitis, favoring GvHD. The patient was started on solumedrol 60mg/day (1 mg/kg) on admission and was continued until 05-Jun-2019. The patient was also started on budesonide 3 mg PO TID on 30-May-2019. Solumedrol was then increased to 60mg BID until 09-Jun-2019 and a taper was started on 10-Jun-2019. The patient was taking prednisone 80 mg PO daily at day of discharge. The skin rash was treated with topical steroids (Desonide and Clobetasol BID starting 27-May-2019) and Mupirocin BID for the hands. The patient was discharged from the hospital on 12-Jun-2019.

The patient was then readmitted on 05-Jul-2019. She had worsening oral intake beginning on 04-Jul-2019 with mid-epigastric pain and diarrhea. She reported that she had skipped two days of tacrolimus secondary to dyspepsia. She reported some nausea, controlled with Zofran as needed. There was no history of bloody stool, emesis, fevers, chills, shortness of breath, chest pain, or urinary symptoms. On examination, her rash appeared most prominently in the same areas in which it had previously appeared. Empiric ceftriaxone had been given prior to admission. The patient's symptoms were consistent with mild GvHD flare and she was started on Solumedrol 30 mg IV (~0.5 mg/kg). She was discharged on 12-Jul-2019. The patient then underwent a biopsy of the colon on 16-Aug-2019 which showed Grade 3-4 GvHD.

The patient was admitted to the hospital on 09-Sep-2019 for failure to thrive, poor appetite, and diarrhea 5 times a day. The patient was then diagnosed with AML relapse based on flow cytometry results on peripheral blood (16-Sep-2019). At the time of admission, the patient was found to show signs of multi-organ failure (pancytopenia, neutropenia, acute blood loss anemia, GI bleeding, coagulopathy, acute GvHD, acidosis, acute renal failure, hepatic failure, respiratory failure, and acute/subacute heart failure). The patient received life-saving medical care in the ICU (epinephrine, norepinephrine, electrolytes, lactate, platelets, packed RBC (PRBC), cryoprecipitate, oxygen, airway management, etc). The patient was also treated with IV antibiotics, antiretroviral, and anti-fungal medications during the hospitalization. On 18-Sep-2019, the patient's multi-organ failure continued to deteriorate in the ICU and she passed away in the hospital on 19-Sep-2019. Primary cause of death was noted as relapse. Autopsy was not performed.

Subject Identifier	GP3SCI-006
Age	42
Sex	Male
Baseline Weight (kg)	113.9
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	19 Jul 2019
Event	Hypoxia
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	03 Dec 2019 – 07 Dec 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3SCI-006 is a 42 year-old White male with Dendritic Cell Leukemia who received an Unmanipulated CBU transplant on 19-Jul-2019.

The patient was diagnosed with Dendritic Cell Leukemia on 12-Dec-2018. He underwent induction therapy with SL 401 cycle 1 on 14-Jan-2019 (completed 4 out of 5 days of treatment), SL 401 cycle 2 on 14-Feb-2019 (discontinued), and four cycles of hyper-CVAD on 11-Mar-2019, 01-Apr-2019, 22-Apr-2019, and 13-May-2019. The patient's past medical history included paroxysmal atrial fibrillation and hypertension. He had severe pulmonary impairment at study screening. Surgical history included hemorrhoidectomy and jaw surgery for realignment.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (15-Jul-2019 to 18-Jul-2019), fludarabine (11-Jul-2019 to 13-Jul-2019), and cyclophosphamide (11-Jul-2019 to 12-Jul-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, fluconazole, levofloxacin, and posaconazole. Neutrophil counts recovered at 24 days post-transplantation (12-Aug-2019). The patient was discharged from the hospital on 13-Aug-2019.

The patient was admitted for workup and management of respiratory failure and acute kidney injury on 03-Dec-2019. The patient presented with shortness of breath, hypoxia (89% on room air), and hypotension (BP 87/64, HR 114). On admission he was tachypneic at 45 bpm and saturating 94% on 2 L nasal canula. The patient became lethargic after receiving hydromorphone for right anterior chest pain.

On 04-Dec-2019 the patient was continued on high-flow nasal canula and felt less short of breath. CT chest showed basilar predominant clustered tree-in-bud and reticulonodular opacities with mosaic attenuation and upper lung predominant multifocal peribronchovascular consolidative and ground-glass opacities. Coronavirus was found to be positive on swab from 04-Dec-2019 and again via bronchoalveolar lavage (BAL) on 06-Dec-2019. Methylprednisolone 80 mg IV (1 mg/kg/day) was started for bronchiolitis obliterans and the patient was

improving on steroids. The patient's oxygen requirement went from 8 L to 3-4 L high-flow nasal canula. The patient was then discharged on 07-Dec-2019.

Subject Identifier	GP3SCI-007
Age	39
Sex	Female
Baseline Weight (kg)	108.6
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	05 Oct 2019
Event	1. Vasovagal Reaction 2. Acute GvHD 3. Sepsis 4. Headaches
Severity	1. Grade 3 2. Grade 4 3. Grade 5 4. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 30 Sep 2019 – 30 Sep 2019 2. 20 Oct 2019 – 26 Nov 2019 3. 24 Nov 2019 – 26 Nov 2019 4. 12 Aug 2019 – 16 Aug 2019
Outcome Of Event	1. Resolved 2. Death 3. Death 4. Resolved
Relationship To The Study Drug	1. NA: Pre-transplant Event 2. Yes 3. No 4. NA: Pre-transplant Event
Date Of Death (If Applicable)	26 Nov 2019

Narrative:
Patient GP3SCI-007 is a 39-year-old White female with ALL who received a Omidubicel transplant on 05-Oct-2019.

The patient was diagnosed with acute lymphoblastic leukemia (Philadelphia chromosome positive ALL) on 03-May-2019. She underwent induction therapy with hyper-CVAD and dasatinib (08-May-2019) and consolidation therapy with blinatumomab and dasatinib (26-Jun-2019). The patient's past medical history included wide complex tachycardia converted with adenosine, anxiety, obesity, and rectal abscess. The patient was hospitalized for headaches from 12-Aug-2019 to 16-Aug-2019. She had four vasovagal/near-syncopal episodes on 30-Sep-2019 due to anxiety for which she was treated with oral lorazepam. She had an additional presyncope event on 07-Oct-2019.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (01-Oct-2019 to 04-Oct-2019), fludarabine 56 mg/day (26-Sep-2019 to 28-Sep-2019), and cyclophosphamide 4176 mg/day (26-Sep-2019 to 27-Sep-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, ciprofloxacin, diaminodiphenyl sulfone, mupirocin topical, and posaconazole. Neutrophil counts recovered at 28 days post-transplantation (02-Nov-2019). The patient was discharged from the hospital on 26-Nov-2019.

On 13-Oct-2019, the patient was noted to have a rash on the face, neck, back, upper chest, and forearms. She was treated with topical steroids but there was no improvement. On 20-Oct-2019, treatment with systemic steroids began. The patient's rash was assessed as diffuse morbilliform eruption with genital involvement, covering 62% of the total body surface area. She required the addition of Patient Controlled Anesthesia on 20-Oct-2019 for perineal pain. The patient had an episode of epistaxis on 16-Oct-2019 which resolved. On 21-Oct-2019, the patient underwent a skin biopsy. Results of the biopsy were consistent with interface dermatitis with adnexal involvement, favoring GvHD. On 24-Oct-2019, the patient's eyelid corners were irritated secondary to topical steroids. There were no vision changes or eye redness.

The patient then developed diarrhea without abdominal pain or cramping. The stool output was approximately 2.4 liters of non-bloody stool. Treatment for diarrhea consisted of diphenoxylate/atropine (Lomotil) four times a day alternating with loperamide (Imodium) four times a day. Octreotide was added on 24-Oct-2019. The patient underwent an esophagogastroduodenoscopy and flexible sigmoidoscopy on 24-Oct-2019. Results from biopsies obtained during the procedure confirmed GvHD. New abdominal pain with associated with abdominal cramping began on 26-Oct-2019. Therefore, the patient was re-staged to Stage 4 GvHD.

The patient was started on tofacitinib on 29-Oct-2019. Tofacitinib was discontinued on 07-Nov-2019. On 06-Nov-2019, the patient reported improvement in abdominal pain and no bowel movements for over 48 hours. Skin GvHD continued to improve with use of triamcinolone twice a day to the body and groin area, desonide to the face and axilla, and clobetasol to the palms with gloves. The patient was also continued on solumedrol. Tacrolimus was held on 04-Nov-2019 due to renal function concerns. Treatment with ruxolitinib (Jakafi) was started on 14-Nov-2019.

On 24-Nov-2019, the patient was noted to be increasingly confused. She had worsening shortness of breath and hypoxia. Her oxygen requirements increased to 6 L and the ICU team was consulted for worsening hypoxia. The patient developed hypotension requiring pressor support, ultimately requiring transfer to the ICU. Initially, the patient required the use of four vasopressors to stabilize her blood pressure, but the team was able to wean her down to two. The patient remained on high-flow oxygen and did not require intubation. She continued to be minimally responsive and minimally followed verbal commands. Blood cultures were obtained and grew gram-negative rods positive for *E. coli*. Vancomycin and meropenem were started for broad-spectrum coverage. The patient showed signs of abdominal pain. CT of the abdomen showed findings consistent with neutropenic colitis. Given her overall clinical picture of sepsis, multi-organ failure and refractory acute GvHD, the decision was made by the family to provide comfort measures only, withdrawing pressor support. The patient passed away on 26-Nov-2019 secondary to sepsis.

Deviations with potential medical significance: The conditioning regimen was not followed per protocol. The start of TBI was one day late. The delay was caused by a serious adverse event.

Subject Identifier	GP3SCI-008
Age	43
Sex	Female
Baseline Weight (kg)	57.6
Race	Unknown
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	13 Sep 2019
Event	*Mycobacterium mucogenicum* Bacteremia
Severity	Grade 2
Serious (Yes/no)	Yes
Start/stop date of Event	13 Dec 2019 – 17 Dec 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	
Narrative:	

Patient GP3SCI-008 is a 43-year-old female with ALL who received an Unmanipulated CBU transplant on 13-Sep-2019.

The patient was diagnosed with ALL on 01-Apr-2019. She underwent induction therapy with E1910 starting on 09-Apr-2019 (randomized trial of combination chemotherapy with blinatumomab versus chemotherapy alone). She received daunorubicin/vincristine on days 1, 8, 15, and 22; intrathecal cytarabine and methotrexate on Day 14; intravenous pegaspargase on Day 18; and dexamethasone 16 mg orally on days 1-7 and 15-21. The patient's past medical history included invasive ductal carcinoma (pT1cN0 L; diagnosed Jun-2016) and depression. Surgical history included left breast lumpectomy (06-Jan-2017).

Prior to the Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (09-Sep-2019 to 12-Sep-2019), fludarabine (05-Sep-2019 to 07-Sep-2019), and cyclophosphamide (05-Sep-2019 to 06-Sep-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, fluconazole, and posaconazole. Neutrophil counts recovered at 20 days post-transplantation (02-Oct-2019). The patient was discharged from the hospital on 03-Oct-2019.

The patient was admitted on 13-Dec-2019 for fevers and *Mycobacterium mucogenicum* bacteremia. She had been having nightly fevers for two weeks, with a maximum temperature of 103°F. She reported feeling "cold" and had a headache associated with the fevers. Blood cultures from 09-Dec-2019 had grown *Mycobacterium mucogenicum* (/ bacilli) in one of four bottles. A CT scan of the chest on 13-Dec-2019 showed the development of numerous small centrilobular nodular opacities in both lungs, concerning for atypical infectious etiology and diffuse interlobular septal thickening compatible with interstitial pulmonary edema. Most nodules were peripheral and non-specific and therefore not concerning for disseminated *Mycobacterium*. A brain MRI with and without contrast on 13-Dec-2019 showed no acute intracranial abnormalities. The patient was treated with imipenem, azithromycin, and trimethoprim-sulfamethoxazole for *Mycobacterium mucogenicum* bacteremia.

The patient continued to have fevers overnight on 14-Dec-2019 with a maximum temperature of approximately 38.5°C. The fevers were down trending on 15-Dec-2019. The patient had new intermittent nausea which was relieved with ondansetron. Repeat blood cultures on 15-Dec-2019 showed no growth. The patient continued to have intermittent nausea and developed diarrhea (stool output ~600 mL over a 24 hour period). The patient was stable and discharged on 17-Dec-2019 at which point the *Mycobacterium mucogenicum* bacteremia was considered resolved.

Subject Identifier	GP3SCI-010
Age	19
Sex	Male
Baseline Weight (kg)	71.0
Race	Asian, Other Southeast Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	22 Nov 2019
Event	1. Pneumonia 2. Multifocal Pneumonia
Severity	1. Grade 3 2. Grade 3
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 10 Jan 2020 – 29 Jan 2020 2. 26 Feb 2020 – 29 Feb 2020
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3SCI-010 is a 19-year-old Asian, Other Southeast Asian male with ALL who received an Unmanipulated CBU transplant on 22-Nov-2019.

The patient was diagnosed with ALL on 11-Apr-2019. He underwent induction therapy with CALGB 10403 course I (16-Apr-2019), consolidation therapy with CALGB 10403 course II (28-May-2019), and maintenance therapy with CALGB 10403 course III (09-Aug-2019). The patient's past medical history included shingles. He had moderate pulmonary impairment at study screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (18-Nov-2019 to 21-Nov-2019), fludarabine (14-Nov-2019 to 16-Nov-2019), and cyclophosphamide (14-Nov-2019 to 15-Nov-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included levofloxacin, acyclovir, and fluconazole. Neutrophil counts recovered at 14 days post-transplantation (06-Dec-2019). The patient was discharged from the hospital on 08-Dec-2019.

On 10-Jan-2020 the patient was admitted for management of pneumonia after a chest X-ray showed findings of pneumonia in the right lower lobe. The patient had been having a cough and nasal congestion over the previous two weeks. He had a fever for two days with a maximum temperature of 102°F which resolved with acetaminophen. The patient also reported three loose to watery bowel movements in the 24 hours prior to admission but denied abdominal pain, nausea, or vomiting. He was treated with cefepime and vancomycin.

On 11-Jan-2020 a chest CT showed bilateral lower lobe pneumonia with greater predominance in the right than left lobe. Levafloxacin was added for atypical coverage. On 12-Jan-2020 the patient had chills and rigors during an IVIG infusion. He was given solumedrol and meperidine with relief and subsequent tolerance of the infusion. A bronchoscopy was performed on 13-Jan-2020. The patient's symptoms improved, and he was discharged on 16-Jan-2020.

The patient was then readmitted on 24-Jan-2020 for worsening pneumonia. Since his discharge the week prior he had continued to have a persistent productive cough and low Grade fever. He also endorsed shortness of breath with exertion. A CT scan of the chest showed worsening nodular ground-glass opacities, most notably in the right lung. The patient received a loading dose of voriconazole and caspofungin 50 mg IV (maintenance dosing) prior to admission. On 25-Jan-2020 the patient had a fever of 100.4°F, persistent cough, and dyspnea on exertion. He was continued on aggressive pulmonary physical therapy and ipratropium bromide/salbutamol (Duoneb) was added. This was changed to just ipratropium bromide (Atrovent) on 26-Jan-2020 due to tachycardia. The patient was stable and discharged on 29-Jan-2020.

The patient was admitted again for pneumonia on 26-Feb-2020. He had a worsening productive cough, rhinorrhea, new onset right pleuritic pain, and desaturation to 92% on room air. Poor air movement was newly noted on exam in the right middle and lower lobes. Upon evaluation in the emergency department, the patient was in no acute distress, saturating at 97-99% on room air, and hemodynamically stable. He had mildly increased work of breathing while talking. Chest CT on 27-Feb-2020 showed new bilateral multifocal areas of centrilobular and tree-in-bud nodularity. A bronchoscopy was performed on 28-Feb-2020. Bronchoalveolar lavage respiratory panel was positive for adenovirus. The patient was treated with cidofovir and IVIG. The patient underwent a repeat bronchoscopy on 29-Feb-2020 and was started on cefepime. Bronchoalveolar lavage returned adenovirus positive so the patient was given an additional dose of cidofovir and IVIG. The patient was otherwise stable and discharged on 29-Feb-2020 with close follow-up.

Subject Identifier	GP3SCI-012
Age	31
Sex	Male
Baseline Weight (kg)	102.0
Race	American Indian or Alaska Native
Study Therapy	Omidubicel
Date Of Study Therapy Administration	22 Nov 2019
Event	Sepsis
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	25 Jun 2020 – 30 Jun 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3SCI-012 is a 31-year-old American Indian or Alaska Native male with ALL who received a Omidubicel transplant on 22-Nov-2019.

The patient was diagnosed with ALL on 27-Jun-2019. He underwent induction therapy with CALGB 10701 with dasatinib and dexamethasone (02-Jul-2019), hyper-CVAD with dasatinib (02-Sep-2019), and hyper-CVAD and dasatinib (14-Oct-2019). The patient's past medical history included right internal jugular thrombus (Oct-2019) and stage IIC (pTxN3S0) germ cell tumor (diagnosed 2012) treated with curative resection and chemotherapy. He had moderate pulmonary impairment (cDLCO = 77) at study screening.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (18-Nov-2019 to 21-Nov-2019), fludarabine (14-Nov-2019 to 16-Nov-2019), and cyclophosphamide (14-Nov-2019 to 15-Nov-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, levofloxacin, and fluconazole. Neutrophil counts recovered at 13 days post-transplantation (05-Dec-2019). The patient was discharged from the hospital on 05-Dec-2019.

The patient presented to the emergency department on 25-Jun-2020 with acute onset nausea, non-bloody vomiting, and 2-3 episodes of non-bloody loose stools. He had a recorded fever at home of 100.5°F. The patient was diagnosed with sepsis and started on piperacillin-tazobactam for presumed intra-abdominal infection. The patient was continued on tacrolimus, prednisone, and dasatinib. CT abdomen/pelvis, urinalysis, and chest X-ray were negative. The patient had improvement in symptoms on 26-Jun-2020 and was discharged home per his request. The plan was to discontinue levofloxacin and have outpatient oncology follow-up. After discharge, the patient still had some nausea and diarrhea. The sepsis event was considered resolved on 30-Jun-2020.

Subject Identifier	GP3SGH-001
Age	22
Sex	Female
Baseline Weight (kg)	61.0
Race	Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	24 Apr 2018
Event	1. Diffuse Alveolar Hemorrhage 2. Type I Respiratory Failure
Severity	1. Grade 4 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 05 May 2018 – 18 May 2018 2. 21 May 2018 – 25 Jul 2018

Outcome Of Event	1. Resolved 2. Death
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	25 Jul 2018

Narrative:
Patient GP3SGH-001 is a 22 year-old Asian female with Acute Biphenotypic Leukemia who received an Unmanipulated CBU transplant on 24-Apr-2018.

The patient was diagnosed with Acute Biphenotypic Leukemia (MLL positive) on 27-Nov-2017. She underwent induction therapy with FLAG-IDA#1 (01-Dec-2017) and FLAG-IDA#2 (29-Dec-2017) and consolidation therapy with HCVAD-B#1 (02-Feb-2018) and HiDAC#1 (02-Mar-2018). The patient's medical history included menorrhagia.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 82 mg/day (19-Apr-2018 to 21-Apr-2018), thiotepa 290 mg/day (17-Apr-2018 to 18-Apr-2018), and busulfan 180 mg/day (19-Apr-2018 to 21-Apr-2018). GvHD prophylaxis with mycophenolate mofetil and cyclosporine was started on 21-Apr-2018. She had PRES with 1st onset seizure on 22-Apr-2018 during the conditioning regimen. She received G-CSF 300 mcg/day from 25-Apr-2018 until engraftment. Infection prophylaxis included acyclovir, ciprofloxacin, cotrimazole, and capsofungin. Neutrophil counts recovered at 16 days post-transplantation (10-May-2018).

Following transplant, the patient had a gram positive bacterial infection on 25-Apr-2018, HHV6 infection on 7-May-2018, right cheek cellulitis on 7-May-2018, and a maxillary sinus infection on 8-May-2018. Her post-transplantation period was also complicated by diffuse alveolar hemorrhage. On 10-May-2018 (+Day 16) the patient experienced central chest discomfort and was noted to have hemoptysis. She subsequently desaturated and the decision was made to transfer her to the ICU. Chest X-ray revealed bilateral alveolar infiltrates. Bronchoscopy showed diffuse erythematous mucosa. Bronchoalveolar lavage (BAL) of the middle lobe was progressively bloody. The patient was intubated and started on methylprednisolone on 10-May-2018 for treatment of diffuse alveolar hemorrhage. She received 3 doses of NovoSeven (Recombinant factor VIIa) on 11-May-2018. The patient's condition then improved and endotracheal tube aspirations become less bloody. The patient was extubated on 18-May-2018 and transferred to the general unit.

The patient subsequently experienced acute desaturation and was reintubated for acute Type I respiratory failure on 21-May-2018. Chest X-ray revealed increased pulmonary infiltrates. Respiratory failure was likely attributed to fluid overload and rhinovirus infection. On 22-May-2018, the patient was extubated. The patient received treatment for fluid overload with IV lasix and potassium chloride (KCL) supplement, and for infection with IV meropenem, IV vancomycin, voriconazole, and foscarnet. She remained under observation in the ICU.

The patient was reintubated on 23-May-2018 due to tachypnea and an FiO2 requirement of 40% while on continuous positive airway pressure. Post-intubation chest X-ray showed improvement of pulmonary infiltrates compared to previous results. Repeat bronchoscopy on 28-May-2018 showed no diffuse alveolar hemorrhage. BAL was positive for rhinovirus and the rest of microbiology was negative. BAL cytology was consistent with drug-induced pneumonitis. A CT chest completed on 30-May-2018 showed extensive bilateral ground-glass change in both lungs associated with centrilobular nodules and mild peribronchial consolidation. The lung changes indicated diffuse airspace disease with a component of small airway involvement. Possible differential considerations included atypical infection (viral, mycobacterial), pulmonary hemorrhage, and graft vs host disease. The patient was broadly covered with antimicrobials but ventilatory settings remained high. She was difficult to wean down despite trials with different ventilatory modes including APRV. Methylprednisolone and cyclosporine were increased for possible immune-mediated cause of persistent Type I respiratory failure. Continuous renal replacement therapy (CRRT) was initiated on 02-Jun-2018 for oliguric acute kidney injury. Right-sided pneumothorax was then observed on chest X-ray on 08-Jun-2018. The patient was on intermittent CRRT and sustained low efficiency dialysis due to acute kidney injury (kidney disease improving global outcomes [KDIGO] Stage 3) until it was stopped on 13-Jun-2018.

On 23-Jun-2018, the patient was noted to have hematemesis and gastroscopy was performed on the same day. Gastroscopy revealed multiple erosions in the antrum and pre-pyloric areas with overlying clots. Hemostasis was achieved with adrenaline injection and clip placement. Hematemesis continued for the next few days and gastroscopy was repeated on 25-Jun-2018. No active upper gastrointestinal bleeding was noted. Recurrent HHV6 viremia was also noted on 25-Jun-2018.

The patient was started on rituximab on 04-Jul-2018 for likely immune-mediated lung injury. The patient was noted to have dermatosis (posterior back) on 08-Jul-2018. Sepsis workup was repeated on 11-Jul-2018 due to poor mentation. Blood cultures on 11-Jul-2018 were positive for Enterococcus faecium and Candida parapsilosa. ID consult was obtained. The patient was started on IV tazocin and daptomycin. She was subsequently switched to IV tazocin, vancomycin, and voriconazole. Meropenem was added in view of hemodynamic instability.

The patient was started on dialysis on 11-Jul-2018 due to non-oliguric acute kidney injury. Ongoing bloody nasogastric (NG) aspirate was also noted occasionally. The patient was on maximum single inotropic support with maximum dose of noradrenaline. The patient's family decided to proceed with cardiopulmonary resusitation (CPR) if needed. Ventilation settings were titrated to maximum settings. There was gradual deterioration. She continued to desaturate despite maximum ventilator settings. CRRT was reinitiated as chest X-ray showed pulmonary congestion and the patient was not producing urine. The patient's blood pressure started to decline despite maximum inotropic support. CRRT was held on 25-Jul-2018 when she was hemodynamically unstable. The family was updated and they decided not to pursue CPR. The patient passed away on 25-Jul-2018. Autopsy was not done. The patient remained intubated until the date of death.

Deviations with potential medical significance: Mycophenolate mofetil was given at 1 g/TID instead of being calculated from the patient's weight as per protocol requirements. The CRA confirmed with the site coordinator that this is the site's practice.

Subject Identifier	GP3SGH-002
Age	16
Sex	Female
Baseline Weight (kg)	56.0
Race	Asian-Vietnamese
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	26 Jun 2018
Event	1. Cerebral Infarction 2. Primary Graft Failure 3. Type 2 Respiratory Failure
Severity	1. Grade 1 2. Grade 3 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 01 Jul 2018 – 07 Jul 2018 2. 28 Jul 2018 – 08 Aug 2018 3. 15 Mar 2019 – 03 May 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Death
Relationship To The Study Drug	1. No 2. Yes 3. No
Date Of Death (If Applicable)	03 May 2019
Narrative:	

Patient GP3SGH-002 is a 16 year-old Asian-Vietnamese female with CML who received an Unmanipulated CBU transplant on 26-Jun-2018.

The patient was diagnosed with CML (chronic phase with no history of blast crisis) on 08-Sep-2015.The patient received initial treatment in her home country. Per her records, the patient was started on imatinib on 01-Oct-2015, however due to increasing platelet and ABl kinase mutation-H396R (Sep-2016) the patient was switched to nilotinib on 21-Sep-2016. Due to rising platelet counts, the patient was discontinued from nilotinib in Nov-2017 and started receiving hydroxyurea (05-Jan-2018 to 14-Mar-2018). The patient subsequently came to the study transplant center and was given dasatinib from 15-Mar-2018 to 18-Jun-2018 before the study transplant. The patient's past medical history also included a congenital atrial septal defect (incidental finding from echo scan performed on 06-Jul-2018).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 72 mg/day (21-Jun-2018 to 23-Jun-2018), thiotepa 250 mg/day (19-Jun-2018 to 20-Jun-2018), and busulfan 156 mg/day (21-Jun-2018 to 23-Jun-2018). GvHD prophylaxis including mycophenolate mofetil and cyclosporine was started on 23-Jun-2018. Infection prophylaxis included acyclovir, cotrimoxazole, ciprofloxacin, posaconazole, levofloxacin, and pentamidine.

The patient was scheduled to receive a double Unmanipulated CBU transplant on 26-Jun-2018. However, towards the end of her first CBU infusion, the patient developed abdominal pain, an intense headache, and hypertension. The infusion was therefore withheld, and the decision was made to discard the remaining product in her tubing. The infusion of the second CBU was postponed to the following day. An urgent CT scan of the brain showed no intracranial abnormalities or bleeding. The patient then received the second CBU infusion on 27-Jun-2018 but developed a headache 15 minutes into the infusion. The patient was administered pain killer and the CBU infusion was temporarily withheld. The cord blood infusion was resumed once her pain had settled. The patient then experienced headache following the infusion and on 28-Jun-2018.

On 01-Jul-2018 (post-transplantation Day +5), the patient was found to be unresponsive with up-rolling eyes and short jerking movements of her body. CT of the brain on 01-Jul-2018 showed a tiny punctate hypodensity in the left caudate head. MRI of the brain on 03-Jul-2018 confirmed a tiny focus of acute infarct in the left caudate head. magnetic resonance angiography (MRA) demonstrated no significant stenosis of the major intracranial arteries. The patient was diagnosed with cerebral infarction on 04-Jul-2018. The patient had a pre-syncopal episode on 05-Jul-2018 with no loss of consciousness. MRI on 06-Jul-2018 showed narrowing of intracranial vessels and new infarction of the right frontal cortex. The patient then developed hypotension, for which tazocin was stopped and switched to meropenem. The patient was switched to sirolimus on 07-Jul-2018 and her symptoms subsequently resolved following the change in immunosuppression. From 07-Jul-2018, the patient had no headaches or new neurological symptoms and the adverse event was considered resolved.

A BM chimerism was then performed on 26-Jul-2018. Results revealed 0% donor mononuclear cells and granulocytes. The patient was confirmed as having a primary graft failure (PGF) on 28-Jul-2018 (post-transplantation Day +32). The patient then underwent a haploidentical transplant on 08-Aug-2018. The patient was admitted to the hospital on 06-Aug-2018 for haploidentical transplant after PGF. Conditioning for haploidentical transplant included TBI 200cGy, fludarabine, cyclophosphamide, and alemtuzumab. The patient had neutrophil engraftment on Day 11 and platelet engraftment on Day 13 following haploidentical transplant. Day 21 chimerism showed 100% donor and 0% BCR/ABL on PCR.

The patient had multiple issues following haploidentical transplant including GI GvHD, candidemia, disseminated adenovirus, and atrial tachycardia. The patient was intubated and admitted to the MICU on 15-Mar-2019 due to worsening Type 2 respiratory failure. Prior to admission to the MICU, the patient was first noted to have subcutaneous emphysema and pneumomediastinum on 30-Dec-2018. The patient's respiratory condition worsened, and the patient was hyperventilating out of proportion to oxygen saturation. The cause of Type 2 respiratory failure was determined to be likely multifactorial with contributions by pulmonary GvHD, hyperchloremic non-anion gap metabolic acidosis, possible bronchiolitis obliterans, neuromuscular weaknesses due to deconditioning and prolonged admission, and Aspergillus tracheobronchitis (noted from endotracheal aspirate on 26-Mar-2019). The patient was started on extracorporeal photopheresis (ECP) as treatment for pulmonary GvHD on 29-Mar-2019 and received IVIG from 20-22 Mar-2019 and on 29-Mar-

2019. The plan was for her to continue receiving IVIG fortnightly from 05-Apr-2019. The patient also underwent right chest wall aspiration/insertion on 04-Apr-2019 due to worsening subcutaneous emphysema. The patient was subsequently extubated on 05-Apr-2019 and was transferred to the general ward on 07-Apr-2019.

The patient was readmitted to the MICU on 10-Apr-2019 as she was unable to keep up with oxygen requirements. The patient underwent tracheostomy on 13-Apr-2019. On 01-May-2019, the patient developed respiratory and metabolic acidosis, and ventilator settings were adjusted, however she was still unable to achieve adequate ventilation. The patient passed away on 03-May-2019. Autopsy was not done. The primary cause of death was noted as primary malignancy, CML, with secondary causes including organ failure (pulmonary) and GvHD.

Deviations with potential medical significance: Mycophenolate mofetil was given at 1 g/TID instead of being calculated from the patient's weight as per protocol requirements. The CRA confirmed with the site coordinator that this is the site's practice.

Subject Identifier	GP3SGH-003
Age	41
Sex	Female
Baseline Weight (kg)	60.3
Race	Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	24-Jul-2018
Event	1. Thrombotic Microangiopathy 2. Graft-Versu- Host Disease - Gut 3. Hepatic veno-occlusive disease 4. Hemorrhagic Cystitis 5. Type 1 Respiratory Failure
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 2 5. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 03 Sep 2018 – 18 Sep 2018 2. 17 Aug 2018 – 07 Nov 2018 3. 27 Aug 2018 - 18 Sep 2018 4. 02 Oct 2018 – 07 Nov 2018 5. 27 Oct 2018 – 07 Nov 2018
Outcome Of Event	1. Resolved 2. Death 3. Resolved 4. Death 5. Death
Relationship To The Study Drug	1. No 2. Yes 3. No 4. No 5. No
Date Of Death (If Applicable)	07-Nov-2018

Narrative:
Patient GP3SGH-003 is a 41 year-old Asian female with AML who received an Unmanipulated CBU transplant on 24-Jul-2018.

The patient was diagnosed with AML [acute monoblastic / acute monocytic leukemia (M5)] on 20-Feb-2018. Induction therapy include cytarabine plus idarubicin 3+7 (23-Feb-2018) and consolidation therapy included cytarabine plus idarubicin 7+2 (23-Mar-2018). The patient's medical history included asthma and epilepsy. The patient had moderate pulmonary impairment at study screening.

Prior to unmanipulated cord blood unit transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 78 mg/day (19-Jul-2018 to 21-Jul-2018), thiotepa 278 mg/day (17-Jul-2018 to 18-Jul-2018), and busulfan 178 mg/day (19-Jul-2018 to 21-Jul-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, ciprofloxacin, posaconazole, cotrimoxazole, and voriconazole. Neutrophil counts recovered at 18 days post-transplantation (11-Aug-2018). The patient was discharged from the hospital on 07-Nov-2018.

The patient's initial hospitalization was prolonged by post-transplant complications including GvHD, veno-occlusive disease (27-Aug-2018 to 18-Sep-2018), thrombotic microangiopathy (03-Sep-2018 to 18-Sep-2018), and hemorrhagic cystitis (02-Oct-2018 to 07-Nov-2018). The patient had multiple infections (Stenotrophomonas bacteremia, HHV6 viremia, CMV viremia, and BK viruria) requiring multiple antibiotic and anti-viral regimens.

The patient was diagnosed with graft-versu- host disease of the gut on 17-Aug-2018. The patient was noted to have diarrhea since 25-Jul-2018. A colonoscopy was scheduled on 15-Aug-2018 to investigate the cause of diarrhea and biopsies were performed. Results of the biopsies on 17-Aug-2018 were consistent with Grade IV acute graft disease. The patient was started on methylprednisolone and doses of immunosuppressants were increased. The patient was also given antithymocyte immunoglobulin from 24-Aug-2018 to 26-Aug-2018 and budesonide from 21-Aug-2018 to 31-Aug-2018. As of 30-Aug-2018, the patient had not responded to the steroids or Anti-Thymocyte Globulin (ATG). CT performed on 31-Aug-2018 showed dilation of the large bowel loop, representing megacolon with no perforation. A rectal tube was inserted on 01-Sep-2018 for decompression. The megacolon was noted to have resolved as of 05-Sep-2018. The patient was still having diarrhea despite NIL by mouth. GI panel PCR on 27-Aug-2018 and 06-Sep-2018 were negative.

The patient was diagnosed with hepatic veno-occlusive disease on 27-Aug-2018. The patient was noted to have "liver swelling" with an increase in bilirubin (total bilirubin- 109 UMOL/L), jaundice, and edema on 27-Aug-2018. Direct Coombs test was negative and no antibodies were detected. The patient was given defibrotide from 27-Aug-2018 to 31-Aug-2018 with resolution of the jaundice. Defibrotide was restarted on 10-Sep-2018 and discontinued on 18-Sep-2018. The patient also underwent a transthoracic echocardiography and an ultrasound (doppler portal/hepatic veins) on the 28-Aug-2018. Ultrasound revealed slightly slow flow in the right portal vein.

As of 10-Sep-2018, the veno-occlusive disease was largely resolved with resolution of generalized edema. Normalization of bilirubin was noted on 18-Sep-2018. Fluid overload responded well to IV furosemide. As of 11-Oct-2018, the patient's gut GvHD was improving and she was noted to have a reduction in the volume of diarrhea. As of 19-Oct-2018, the patient was noted to have increasing small volume diarrhea. A colonoscopy was performed on 19-Oct-2018 for further investigation and there was no evidence of CMV colitis.

The patient was then noted to have a more distended abdomen on 25-Oct-2018. CT abdomen done on 26-Oct-2018 revealed small bowel obstruction, mild edema of the distal ileum, possible ileus, and the development of moderate right hydroureteronephrosis. The patient was noted to have progressive abdominal distension and melena starting 26-Oct-2018. Endoscopy was performed on 01-Nov-2018 which revealed multiple gastric ulcers and duodenitis. Ileus and slow gastrointestinal bleeding were likely secondary to gut GvHD. Budesonide was given from 10-Oct-2018 until 22-Oct-2018. The patient was also given ruxolitinib from 23-Oct-2018 to 24-Oct-2018 which was stopped due to low counts.

The patient was intubated and transferred to the MICU on 27-Oct-2018 for management of Type 1 Respiratory Failure. The patient was started on Airway pressure release ventilation (APRV) in the MICU. The CT scan performed on 26-Oct-2018 had revealed patchy consolidations in both lungs, representing a chest infection. Bronchoscopy was performed on 27-Oct-2018 which showed no endobronchial lesions in the airways. BAL culture reports were negative. Blood cultures were also negative. Chest X-ray on 27-Oct-2018 showed interval appearance of extensive airspace consolidation in both lungs (noted progression of left upper lobe (LUL) and right upper lobe (RUL) consolidation from CT done on 26-Oct-2018). Improvement in the left lung opacity was seen in repeat chest X-ray done on 28-Oct-2018 and no pneumothorax was seen. Type 1 respiratory failure was presumed likely secondary to hospital acquired pneumonia with ARDS vs fluid overload vs TRALI. The patient had a breakthrough seizure on Keppra on 28-Oct-2018 secondary to acute illness.

The patient's ventilatory requirements improved over the next three days, and the patient was weaned to pressure support ventilation. Serial chest x-rays showed significant improvement, raising the possibility of TRALI. However, the patient still required moderate PEEP. A workup for TRALI was performed on 29-Oct-2018. The patient was not stable enough to undergo a CT PA.

On 05-Nov-2018, the patient was noted to be deteriorating clinically. Due to decreasing oxygenation and increasing ventilator support, paralysis was initiated. The patient was also noted to have a fever on 03-Nov-2018 and 04-Nov-2018. On 07-Nov-2018, the patient's blood pressure was down trending despite dual inotropic support. The patient's family was updated and they decided not to resuscitate. The patient passed away on 07-Nov-2018. The cause of death was noted as adult respiratory distress syndrome, other than IPS, secondary to pneumonia. Autopsy was not done.

Deviations with potential medical significance: Per the infusion Summary form, the site transplanted intended treatment CBU #1 (070368). However, on infusion day, backup CBU #1 (0719203214) was infused instead of intended treatment CBU #2 (1219219934), as the backup unit had a higher cell dose. As this happened more than 2 years ago, the site could not recall the actual event (i.e. whether the change in decision regarding the CBU was done before or after randomization). Emmes project leader Steve Wease confirmed via email on 14-Oct-2020 that this would be considered a minor protocol deviation.

Subject Identifier	GP3SGH-004
Age	18
Sex	Male
Baseline Weight (kg)	63.0
Race	Asian - Other Southeast Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	23 Aug 2018
Event	Abdominal pain
Severity	Grade 1
Serious (Yes/no)	Yes
Start/stop date of Event	27 Oct 2018 – 29 Oct 2018
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3SGH-004 is an 18 year-old Asian - Other Southeast Asian male with lymphoma who received an Unmanipulated CBU transplant on 23-Aug-2018.

The patient was diagnosed with lymphoma on 25-Aug-2017. He underwent treatment with six cycles of CHOPE (25-Aug-2017 to 08-Dec-2017), 12 rounds of intrathecal methotrexate (12-Sep-2017 to 01-Dec-2017), one cycle of DHAP (11-Jan-2018), two cycles of brentuximab (05-Feb-2018 to 26-Feb-2018), and alectinib (14-Mar-2018). There was no additional reported past medical history.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (18-Aug-2018 to 20-Aug-2018), thiotepa (16-Aug-2018 to 17-Aug-2018), and busulfan (18-Aug-2018 to 20-Aug-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included posaconazole, acyclovir, ciprofloxacin, oseltamivir, and cotrimoxazole. Neutrophil counts recovered at 19 days post-transplantation (11-Sep-2018). The patient was discharged from the hospital on 20-Sep-2018.

The patient experienced generalized abdominal crampy pain, primarily in the periumbilical region, on 27-Oct-2018. The patient visited the emergency department after an increase in the severity of pain and was admitted on 28-Oct-2018. On admission he was given 50mg tramadol for pain relief. The pain was relieved partially with panadol/tramadol and resolved on 29-Oct-2018. No abnormalities were noted on abdominal X-ray (28-Oct-2018). The event was considered likely secondary to constipation and the patient was discharged on 29-Oct-2018.

Subject Identifier	GP3SGH-006
Age	23
Sex	Male
Baseline Weight (kg)	90.9
Race	Asian – Other Southeast Asian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	26 Aug 2019
Event	Methicillin-resistant Staphylococcus aureus (MRSA) Infection
Severity	Grade 3
Serious (Yes/no)	Yes
Start/stop date of Event	30 Jun 2020 – 12 Jul 2020
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3SGH-006 is a 23 year-old Asian, other Southeast Asian male with AML who received a Omidubicel transplant on 26-Aug-2019.

The patient was diagnosed with AML on 20-Jul-2017. He underwent induction therapy with IA 3+7 (27-Jul-2017), consolidation therapy with three cycles of HiDAC (cycle #1: 24-Aug-2017; cycle #2: 19-Sep-2017; cycle #3: 19-Oct-2017), maintenance therapy with azacitidine (Nov-2017 to May-2018), and reinduction therapy with two cycles of FLAG (cycle #1: 16-Apr-2019; cycle #2: 31-May-2019).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (21-Aug-2019 to 23-Aug-2019), thiotepa (19-Aug-2019 to 20-Aug-2019), and busulfan (20-Aug-2019 to 22-Aug-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, cotrimoxazole, posaconazole, voriconazole, and ciprofloxacin. Neutrophil counts recovered at seven days post-transplantation (02-Sep-2019). The patient was discharged from the hospital on 06-Sep-2019.

The patient was noted to have right ear otitis externa and right thigh cellulitis on 29-Jun-2020. He was subsequently admitted on 30-Jun-2020 for treatment with intravenous (IV) antibiotics. The patient received IV piperacillin-tazobactam during admission. Blood cultures for aerobic/anaerobic bacteria were done on 29-Jun-2020 with no growth detected. Pus swab performed on 03-Jul-2020 was positive for MRSA. The patient was discharged on 06-Jul-2020 to complete treatment with oral clindamycin. The clindamycin course was completed on 12-Jul-2020 at which point the MRSA event was considered resolved.

Subject Identifier	GP3SGH-007
Age	51
Sex	Male
Baseline Weight (kg)	73.5
Race	Asian – Other Southeast Asian
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	21 Jan 2020
Event	1. HHV6 Viremia 2. Chromosomal Translocation 3. Disease Relapse
Severity	1. Grade 2 2. Grade 2 3. Grade 5
Serious (Yes/no)	1. Yes 2. Yes

	3. Yes
Start/stop date of Event	1. 19 Feb 2020 – 28 Feb 2020 2. 20 Feb 2020 – 26 Mar 2020 3. 24 Mar 2020 – 01 Apr 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Death
Relationship To The Study Drug	1. No 2. Yes 3. No
Date Of Death (If Applicable)	01 Apr 2020

Narrative:
Patient GP3SGH-007 is a 51-year-old Asian, Other Southeast Asian male with AML who received an Unmanipulated CBU transplant on 21-Jan-2020.

The patient was diagnosed with AML (with maturation – M2) on 11-Jun-2018. He underwent induction therapy with IA 3+7 (02-Jul-2018) and consolidation therapy with HiDAC #1 (21-Aug-2018), HiDAC #2 (25-Sep-2018), and HiDAC #3 (23-Oct-2018). The patient relapsed in July 2019 (FLT3/NPM/CEBPA positive). He received reinduction and salvage therapy with FLAG/idarubicin (29-Jul-2019) and FLAG (14-Oct-2019). Maintenance therapy included azacitadine (02-Dec-2019 to 10-Dec-2019). The patient's past medical history included Hepatitis B (1999) and G6PD deficiency.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 88 mg/day (16-Jan-2020 to 18-Jan-2020), thiotepa 327 mg/day (14-Jan-2020 to 15-Jan-2020), and busulfan 210 mg/day (15-Jan-2020 to 17-Jan-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir and posaconazole. Neutrophil counts recovered at 18 days post-transplantation (08-Feb-2020). The patient was discharged from the hospital on 13-Feb-2020.

The patient was seen for a post-transplantation follow-up visit on 19-Feb-2020 and was subsequently readmitted for asymptomatic HHV6 viremia. His HHV6 levels were rising from 3.0 copies/ml on 13-Feb-2020, to 3.43 copies/ml on 17-Feb-2020, to 3.04 copies/ml on 19-Feb-2020. The patient was started on intravenous (IV) foscarnet. A BM aspiration was performed on 20-Feb-2020. Karyotyping results showed that there was a translocation between chromosomes 1 and 11. This abnormality was not present prior to transplant. It was not known for sure if the t(1;11) abnormality was from the donor or recipient, though it was more likely from the donor since the variable number tandem repeat (VNTR) was 100% donor. The Cord Blood Bank was contacted through the donor registry for further evaluation, but no additional information was provided. HHV6 then became undetectable on both 24-Feb-2020 and 27-Feb-2020. IV foscarnet was discontinued on 27-Feb-2020. The patient was discharged on 28-Feb-2020.

On 24-Mar-2020, the patient was seen in clinic for routine blood work and was noted to have a fever of 38.1°C. The patient was unaware of the fever until his temperature was taken and reported no other symptoms. Due to the fever, the patient was admitted, and blood and urine tests were done. Blood cultures (aerobic) and urine cultures performed on 24-Mar-2020 were negative.

On 26-Mar-2020, full blood count results for the patient showed presence of blast cells (5%). A BM aspirate/biopsy was performed on the same day and preliminary results from the BM revealed presence of 85% blast cells, indicative of disease relapse. The fever reported previously was considered likely a malignant fever secondary to relapse. On 31-Mar-2020, the patient was noted to have left eye subconjunctival hemorrhage and peri-orbital hematoma with intermittent headache. On 01-Apr-2020, the patient became unresponsive yet semi-conscious. A CT scan was performed and indicated a moderate-sized acute subdural hematoma. The patient rapidly deteriorated and passed away on 01-Apr-2020. Primary cause of death was noted to be subdural hemorrhage and secondary cause was noted as disease relapse.

Deviations with potential medical significance: The patient was not prescribed or administered any anti-bacterial prophylaxis due to G6PD deficiency. As per protocol, anti-bacterial prophylaxis is required.

Subject Identifier	GP3TAS-001
Age	39
Sex	Female
Baseline Weight (kg)	70.0
Race	White – European
Study Therapy	Omidubicel
Date Of Study Therapy Administration	20 Aug 2019
Event	CMV Reactivation
Severity	Grade 2
Serious (Yes/no)	Yes
Start/stop date of Event	18 Sep 2019 – 03 Oct 2019
Outcome Of Event	Resolved
Relationship To The Study Drug	No
Date Of Death (If Applicable)	

Narrative:
Patient GP3TAS-001 is a 39 year-old White, European female with ALL who received a Omidubicel transplant on 20-Aug-2019.

The patient was diagnosed with ALL, with CNS involvement, on 25-Mar-2019. She underwent two cycles of induction therapy according to protocol GRAAPH 2005 on 26-Mar-2019 and 07-May-2019. Consolidation therapy with 12 intrathecal injections of methotrexate and cytarabine were given from 01-Apr-2020 through 27-Jun-2019. The patient's past medical history included anxiety, hypothyroidism, carpal tunnel syndrome, patent foramen ovale, and HSV1 reactivation. She had mild hepatic impairment (AST 80 U/L) at study screening. The patient had a reported allergy to amoxicillin/clavulanic (Augmentin).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of thiotepa 292 mg/day (13-Aug-2019 to 14-Aug-2019), fludarabine 81.5 mg/day (15-Aug-2019 to 17-Aug-2019), and busulfan 187 mg/day (15-Aug-2019 to 17-Aug-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, trimethoprim/sulfamethoxazole, and ciprofloxacin. Neutrophil counts recovered at 16 days post-transplantation (05-Sep-2019). The patient was discharged from the hospital on 12-Sep-2019.

The patient was admitted on 18-Sep-2019 for management of CMV reactivation. A previous CMV viral load on 15-Sep-2019 had been 2537 IU/mL. On 22-Sep-2019, CMV levels went up to 5557 IU/mL. The patient received treatment with foscarnet and valganciclovir. The CMV viral load was zero on 03-Oct-2019 at which point the CMV reactivation event was considered resolved.

Subject identifier	GP3UMN-001
Age	23
Sex	Male
Baseline weight (kg)	87.1
Race	Caucasian
Study therapy	Omidubicel
Date of study therapy administration	17 May 2018
Event	1. Acute GvHD 2. Lung Infection 3. Acute GvHD Flare 4. Soft Tissue Infection
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3
Serious (yes/no)	1. Yes

	2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 08 Aug 2018 – 03 Oct 2018 2. 28 Jan 2019 – 02 Feb 2019 3. 08 Feb 2019 – 21 Feb 2019 4. 23 Feb 2019 – 11 Mar 2019
Outcome of event	1. Resolved 2. Resolved with sequelae 3. Resolved with sequelae 4. Resolved
Relationship to the study drug	1. Yes 2. No 3. Yes 4. No
Date of death (if applicable)	

Narrative:
Participant GP3UMN-001 is a 23 year-old Caucasian male with Acute Lymphoblastic Leukemia who received an omidubicel transplant on 17-May-2018.

The participant was diagnosed with Acute Lymphoblastic Leukemia (subtype Precursor T-cell ALL, extramedullary involvement to anterior mediastinal region) on 11-Dec-2017. He was treated with PETHEMA protocol from Dec-2017 to Mar-2018. His past medical history included atrial fibrillation, GERD, depression, anxiety, and ADHD. He had a history of severe pulmonary dysfunction (respiratory failure in Dec-2017 that required oxygen) and an elevated ALT that were not present at study screening. The participant was antibody positive for EBV IgG and CMV antibodies at screening.

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of total body irradiation 165 cGy twice daily (13-May-2018 to 16-May-2018), fludarabine 54 mg/day (09-May-2018 to 11-May-2018), and cyclophosphamide 5425 mg/day (09-May-2018 to 10-May-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Neutrophil counts recovered at eight days post-transplantation (25-May-2018). The participant was discharged from the hospital on 13-Jun-2018.

The participant was admitted to the hospital on 08-Aug-2018 for management of acute GvHD. The participant had acute GvHD symptoms initially starting on 06-Jun-2018 and had been treated with steroids and Pregnyl. He was started on budesonide on 07-Aug-2018 and was on a prednisone taper at the time of his admission. The participant was admitted to the hospital with worsening gastrointestinal symptoms, an inability to tolerate oral intake, and a 5kg weight loss since his transplant. He had a skin rash that had worsened which covered 50% of his body surface area. On 09-Aug-2018, a duodenal biopsy was found to be negative for acute GvHD while gastric biopsy showed grade I GvHD. The participant was continued on prednisone 60mg PO daily. The participant was discharged on 11-Aug-2018 to continue care in the outpatient clinic. On 01-Oct-2018, the participant was re-admitted to the inpatient unit with an acute GvHD flare. The participant was treated with increased steroids and discharged on 03-Oct-2018. The acute GvHD events were reported as resolved as of 03-Oct-2018.

The participant then had a lung infection (presumed fungal) from 28-Jan-2019 to 02-Feb-2019. He was then admitted again on 08-Feb-2019 for management of acute GvHD flare. The participant presented with a 10-day history of diarrhea, some abdominal cramping, and a loss of appetite. He had been recently diagnosed with norovirus (27-Jan-2019) for which he was treated with nitazoxanide 500mg twice daily. The participant was admitted to the hospital on 08-Feb-2019 because of ongoing norovirus and GvHD. On admission, the participant was found to have elevated liver function tests (ALT: 103 U/L, AST: 52 U/L, ALKP: 184 U/L) but total bilirubin was within normal limits (0.5 mg/dL). The participant refused a liver biopsy but underwent flexible sigmoidoscopy on 11-Feb-2019 which showed grade I GvHD. The participant did not improve with conservative management, so he was started on methylprednisone 48 mg/m2 with substantial clinical

improvement. The BMT team considered starting the participant on Jakafi as well but with ongoing presumed fungal pneumonia the choice was made to not pursue Jakafi.

The participant was then planned for discharge on 21-Feb-2019. Incidentally, three hours before the discharge, EBV testing came back at a million copies. A CT chest/abdomen/pelvis was done which showed prominence of lymph nodes and there was a suspicion for post-transplant lymphoproliferative disorder (PTLD). Since the mediastinal and retroperitoneal lymph nodes were too small, biopsy was not recommended. Instead, the plan was to do a liver biopsy. The participant refused to extend his hospital stay and wanted to be discharged. He also had desaturation on walking to 88% on discharge day and hence was discharged with oxygen as needed (PRN). At home, the participant had progressively worsening throat and ear pain, and was readmitted to the hospital for a soft tissue infection on 23-Feb-2019. During this re-admission, the liver biopsy was negative for PTLD and GvHD. The acute GvHD flare was therefore considered resolved with sequelae on 21-Feb-2019.

During the Long Term Follow-up, a biopsy of a right frontal tumor on 22-Jan-2020 (day +615) revealed monomorphic PTLD, EBV-positive diffuse large B-cell lymphoma. Treatment was given with rituximab, ibrutinib, and radiation until 27-Feb-2020. Daily ibrutinib was discontinued due to possible GI toxicity. As of 12-May-2020, a bone marrow exam revealed 100% donor chimerism. An MRI scan performed on 11-Nov-2020 showed remission status, and the blood EBV test was negative on 04-Jan-2021. There is no report of progression up to the last follow-up, approximately four months before the cut off.

Subject Identifier	GP3UMN-002
Age	54
Sex	Male
Baseline Weight (kg)	84.4
Race	Native Pacific Islander
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	19 Apr 2018
Event	No events
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	

Narrative:
Patient GP3UMN-002 is a 54 year-old Native Pacific Islander male with ALL who received an Unmanipulated CBU transplant on 19-Apr-2018.

The patient was diagnosed with Philadelphia chromosome positive ALL on 15-Nov-2017. He underwent induction therapy with GRAAL (2005) and hyper-CVAD 1B. Maintenance therapy included one cycle of hyper-CVAD. The patient's past medical history included anal fissure, hemorrhoids, and cardiac morbidity. His surgical history included two cardiac stents, varicocelectomy, and dental extraction.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (15-Apr-2018 to 18-Apr-2018), fludarabine (11-Apr-2018 to 13-Apr-2018), and cyclophosphamide (11-Apr-2018 to 12-Apr-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, fluconazole, and levofloxacin. Neutrophil counts recovered at 15 days post-transplantation (04-May-2018). The patient was discharged from the hospital on 29-May-2018. The patient had no reported SAEs post-transplantation.

Subject Identifier	GP3UMN-003
Age	55
Sex	Female
Baseline Weight (kg)	83.9
Race	White – North American
Study Therapy	Omidubicel
Date Of Study Therapy Administration	18 May 2018
Event	No events
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	

Narrative:
Patient GP3UMN-003 is a 55 year-old White, North American female with AML who received a Omidubicel transplant on 18-May-2018.

The patient was diagnosed with AML on 29-Sep-2016. She underwent induction therapy with 7+ 3 from 30-Sep-2016 to 06-Oct-2016 and a second induction on 22-Jan-2018. Consolidation therapy included HiDAC 3 g/m^2 (16-Nov-2016), HiDAC 1 g/m^2 (16-Dec-2016), cycle #1 (04-Nov-2016 to 08-Nov-2016), cycle #2 (02-Dec-2016 to 06-Dec-2016), cycle #3 (13-Feb-2017 to 18-Feb-2017), and cycle 4 (14-Mar-2017 to 18-Mar-2017). Reinduction included 7+3 (23-Jan-2018 to 29-Jan-2018) and consolidation cycle 1 with MIDAC (02-Mar-2018 to 05-Mar-2018). The patient's past medical history included bipolar II disorder and diabetes mellitus Type 2 (22-Sep-2016). The patient's surgical history included parathyroidectomy (03-Aug-2017).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (14-May-2018 to 17-May-2018), fludarabine (10-May-2018 to 12-May-2018), and cyclophosphamide (10-May-2018 to 11-May-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, fluconazole, levofloxacin, and vancomycin. Neutrophil counts recovered at 15 days post-transplantation (02-Jun-2018). The patient was discharged from the hospital on 14-Jun-2018. The patient had no reported SAEs post-transplantation.

Subject Identifier	GP3UMN-004
Age	45
Sex	Male
Baseline Weight (kg)	73.3
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	20 Jul 2018
Event	Relapsed B-Cell ALL
Severity	Grade 5
Serious (Yes/no)	Yes
Start/stop date of Event	24 Oct 2018 – 19 Jun 2019
Outcome Of Event	Death
Relationship To The Study Drug	No
Date Of Death (If Applicable)	19 Jun 2019

Narrative:
Patient GP3UMN-004 is a 45 year-old White male with ALL who received a Omidubicel transplant on 20-Jul-2018.

The patient was diagnosed with acute lymphoblastic leukemia (Precursor B-Cell ALL) on 25-Feb-2015. His treatment included induction with one cycle hyper-CVAD (26-Feb-2015) and one cycle PETHEMA (29-Apr-

2015), consolidation with vincristine, methotrexate, cytarabine (Ara-C), PEG asparagase, cyclophosphamide, and decadron (25-Mar-2015), maintenance with MP6 (methotrexate, prednisone, and 6-Mercaptopurine; 15-Sep-2015 to 29-Aug-2017), and reinduction with blinatumomab (6-Feb-2018), Ara-C MP3 (09-Mar-2018), Inotuzumab (25-Apr-2018 to 30-May-2018), and triple intrathecal therapy with hydrocortisone, methotrexate, and Ara-C (9-Mar-2018). His past medical history included anxiety treated with Xanax, bell's palsy, reflux esophagitis, ruptured lumbar disc, and sciatica. At screening he had mild hepatic impairment. Surgical history included bilateral inguinal orchiectomy (2017).

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (16-Jul-2018 to 19-Jul-2018), fludarabine 52 mg/day (12-Jul-2018 to 14-Jul-2018), and cyclophosphamide 5370 mg/day (12-Jul-2018 to 13-Jul-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Neutrophil counts recovered at 7 days post-transplantation (27-Jul-2018). The patient was discharged from the hospital on 31-Jul-2018.

On 9-Aug-2018 (post-transplantation day +21) the patient's BM showed no morphologic or immunophenotypic evidence of B-lymphoblastic leukemia. Flow cytometry showed no abnormal B lymphoblast populations and FISH was cancelled due to negative flow cytometry/morphology and 100% donor cells. On 24-Oct-2018, a BM biopsy was normal morphologically, 100% donor, but a population of abnormal B cells at 0.2% was identified by flow cytometry. The abnormal B cell population was likely consistent with MRD. The patient was then diagnosed with Relapsed B-Cell ALL on 24-Oct-2018 (post-transplantation day +100). The patient was started on blinatumomab on 02-Nov-2018 and returned to his home clinic for further treatment.

The patient was admitted on 22-Feb-2019 for a course of lymphodepleting therapy. The patient was then scheduled to receive a Zuma 3 trial CAR-T infusion on 08-Mar-2019 but was admitted on 07-Mar-2019 for infectious management of cellulitis and a fluid collection near his Hickman catheter. Fluid from the area was aspirated but there was not enough to test for infection or growth. Blood cultures were negative. The patient's erythema and tenderness improved with vancomycin, which was started the morning of 07-Mar-2019. Infectious diseases reviewed the case and recommended removal of the Hickman catheter and continuation of IV antibiotic therapy for 7 days. The catheter was removed. The patient received vancomycin through 12-Mar-2019 with transition to daptomycin on 13-Mar-2019. The patient's CAR-T-cell infusion, as part of the Zuma 3 trial for ALL, was deferred until he completed the therapeutic antibiotic course. He remained afebrile and blood cultures from admission remained negative. A Hickman catheter was then placed on 14-Mar-2019. The patient received his Day 0 CAR-T infusion on 15-Mar-2019. He remained hospitalized through Day +7 of CAR-T. He was then discharged on 23-Mar-2019 and was asked to continue with outpatient follow-up through Day +30.

The patient was then admitted to an outside hospital with epistaxis and was treated with platelets. Severe thrombocytopenia was noted as well as life-threatening coagulopathy due to suspected sepsis. The Palliative Care team recommended hospice as there was no curative-intent or life prolonging therapy that would be compatible with quality of life. The patient was placed on comfort measures and passed away on 19-Jun-2019. Primary cause of death was noted as relapse/progression of disease. Autopsy was not done.

Subject identifier	GP3UMN-005
Age	53
Sex	Male
Baseline weight (kg)	90.8
Race	White – North American
Study therapy	Omidubicel
Date of study therapy administration	07 Nov 2018
Event	1. Acute GvHD 2. Disease Relapse
Severity	1. Grade 1 2. Grade 4

Serious (yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 04 Jan 2019 – 22 May 2019 2. 15 Aug 2019 – 07 Nov 2019
Outcome of event	1. Resolved 2. Resolved by convention
Relationship to the study drug	1. Yes 2. No
Date of death (if applicable)	30 Jun 2020

Narrative:
Participant GP3UMN-005 is a 53 year-old White, North American male with Acute Lymphoblastic Leukemia who received an omidubicel transplant on 07-Nov-2018.

The participant was diagnosed with Acute Lymphoblastic Leukemia (Precursor B-Cell ALL) on 26-Jun-2017. He underwent induction therapy with PETHEMA (28-Jun-2017), three cycles of early consolidation therapy (09-Aug-2017 to 16-Oct-2017), four cycles of delayed consolidation therapy (13-Nov-2017 to Jun-2018; relapse during cycle 4 with flow cytometry positive for blasts in the CNS), and reinduction therapy with hyper-CVAD cycle 1B with 6-mercaptopurine orally and intrathecal methotrexate. The participant's past medical history included kidney stones, cardiac impairment, moderate pulmonary impairment, and rhizopus and acid-fast bacillus (AFB) infections requiring continuation of intravenous (IV) antimicrobial treatment at study screening. Surgical history included thoracoscopic wedge surgery (06-Jul-2018).

Prior to omidubicel transplant, the participant was treated with a myeloablative conditioning regimen consisting of total body irradiation 165 cGy/day (03-Nov-2018 to 06-Nov-2018), fludarabine 58 mg/day (30-Oct-2018 to 01-Nov-2018), and cyclophosphamide 6000 mg/day (30-Oct-2018 to 31-Oct-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir and posaconazole. Neutrophil counts recovered at 17 days post-transplantation (24-Nov-2018). The participant was discharged from the hospital on 26-Nov-2018.

The participant was diagnosed with acute GvHD on 04-Jan-2019. The participant presented with a seven-day history of increased nausea and diarrhea. Upper and lower endoscopies were performed on 03-Jan-2019 with results positive for acute GvHD of the stomach, sigmoid colon, and rectum. Acute GvHD scores were: Skin 0, Upper GI 1, Lower GI 1, Liver 0, and overall Grade 1. The participant was started on prednisone at 60mg/m2/day (45mg/QID) on 04-Jan-2019. Steroid taper was completed on 27-Mar-2019. As of 23-Apr-2019, GvHD symptoms were ongoing but the participant was no longer on systemic steroids. A skin biopsy was performed on 22-Apr-2019, and topical steroids were initiated for a new rash to the face, chest, and shoulders. The participant was seen on 22-May-2019 and reported intermittent GI symptoms, but these were thought to not be consistent with GvHD. The acute GvHD event was reported as resolved as of 22-May-2019.

The participant was then seen on 20-Aug-2019 for concerns of dropping platelet counts and a small population of abnormal cells noted on peripheral blood flow cytometry on 15-Aug-2019. Bone marrow biopsy was obtained on 20-Aug-2019 which showed persistent/recurrent acute leukemia involving approximately 46% of markedly hypercellular bone marrow (80% cellular). The participant was confirmed as having disease relapse and was sent home to consider the option of finding a center with an open trial using CAR-T therapy.

The participant returned to the study center on 26-Aug-2019 for re-induction therapy. The treatment plan was to continue intrathecal chemo twice weekly until there were two consecutive negative blast counts in CSF, then do weekly chemo until three consecutive negative blast counts in CSF. The participant completed inotuzumab cycle 1, including inotuzumab 0.8 mg/m2 on 26-Aug-2019 (Day 1) and inotuzumab 0.5 mg/m2 on 02-Sep-2019 (Day 8), without any complications. He was discharged home on 05-Sep-2019.

Bone marrow biopsy on 09-Oct-2019 showed no morphological evidence of acute leukemia. Flow cytometry from the bone marrow on 09-Oct-2019 showed 0.06% of cells that were suspicious for abnormal blast. This was reviewed by a pathologist and a more definitive confirmation of abnormal blasts could not be concluded. The disease relapse event was resolved by convention on 07-Nov-2019 (post-transplantation day +365). To

that date, the participant had no additional admissions. The participant as of 12-Nov-2019 was going to be screened for CAR-T trial and if unable to enroll had plans for another cord blood unit transplant.

The participant died on 30-Jun-2020 due to disease relapse.

Subject Identifier	GP3UMN-006
Age	55
Sex	Male
Baseline Weight (Kg)	69.7
Race	White – North American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	07 Dec 2018
Event	1. Infusion-Related Reaction 2. Acute GvHD 3. C. Difficile Infection
Severity	1. Grade 3 2. Grade 2 3. Grade 2
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 07 Dec 2018 – 07 De 2019 2. 03 Jan 2019 – 18 Jan 2019 3. 04 Jun 2019 – 07 Jun 2019
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved
Relationship To The Study Drug	1. Yes 2. Yes 3. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3UMN-006 is a 55 year-old White, North American male with Myelodysplastic Syndrome who received an unmanipulated CBU transplant on 07-Dec-2018.

The patient was diagnosed with Myelodysplastic Syndrome (refractory cytopenia with multilineage dysplasia - RCMD) on 22-May-2014. He underwent induction therapy with five cycles of azacitidine (18-Jun-2018 to 02-Nov-2018). The patient's past medical history included Grade 2 anxiety and depression (2000), chronic sinusitis, sweet syndrome, left thigh nodule, and Grade 2 elevated QTc. His surgical history included right hernia repair (2002). The patient had reported allergies to codeine, Bactrim, claritin, and singulair.

Prior to unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI 165 cGy/day (03-Dec-2018 to 06-Dec-2018), fludarabine 45 mg/day (29-Nov-2018 to 01-Dec-2018), and cyclophosphamide 4190 mg/day (29-Nov-2018 to 30-Nov-2018). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, levofloxacin, micafungin, voriconazole, posaconazole, and piperacillin-tazobactam. Neutrophil counts recovered at 16 days post-transplantation (23-Dec-2018). The patient was discharged from the hospital on 18-Jan-2019.

The patient experienced an infusion-related reaction during the study product infusion on 07-Dec-2018. Following premedication with 50 mg oral diphenhydramine, 50 mg solu-cortef, and 650 mg oral acetaminophen, the infusion of cord blood cells was started. Six minutes into the infusion, the patient reported feeling anxious and developed a seizure witnessed by the physician that lasted for < 5 min and resolved with intravenous lorazepam. Upon recovery, the patient was non-focal, conscious, and conversant. He had a stat neurology evaluation and was started on levetiracetam. EEG was within normal limits and brain MRI was

normal. There were no recurrent seizures. The patient also reported diffuse pruritus and developed a maculopapular rash. He received additional doses of diphenhydramine and steroids.

The cord blood infusion was restarted and resulted in recurrence of skin symptoms. Additional doses of diphenhydramine and steroids were required to complete the infusion of cord blood cells. The rash resolved with completion of the cord blood infusion. The patient reported chest pain and pressure during infusion. He did not require any specific cardiac interventions. Evaluation with EKG and serial troponins did not demonstrate any cardiac injury. The patient had transient hypotension Grade 3 after each dose of diphenhydramine which was responsive to intravenous fluids. Per the site's clinical routine, blood cultures were sent. The blood cultures came back positive with gram positive cocci in cluster > 72h after the event, and the patient was started on appropriate antibiotics. Samples taken from the bags of the cord blood products were sent for culture and were negative to date. The patient remained stable and afebrile. The infusion-related reaction was considered resolved on 07-Dec-2018 and there were no permanent sequelae to the reaction.

On 02-Jan-2019, a skin biopsy done on 28-Dec-2018 for a rash covering 18% of the patient's body surface area was found to be positive for acute GvHD. The rash covered 50% of the patient's body surface area on the date of diagnosis and was treated with topical steroid cream. The patient also had a reported history from 22-Dec-2019 of anorexia and persistent nausea, with TPN dependence. The patient also reported loose stool. He had a recent history of *C. difficile* infection (last culture on 01-Jan-2019 was reported as negative). Upper and lower endoscopy scopes performed on 03-Jan-2019 confirmed acute GvHD in the duodenum, esophagus, and sigmoid colon. The patient was started on methylprednisolone 48 mg/m2/day (29 mg IV QID) on 03-Jan-2019. Acute GvHD scores were: Skin 2, Upper GI 1, Lower GI 1, Liver 0, and an overall Grade of 2. The patient was continued on sirolimus and mycophenolate mofetil. The patient was discharged from the inpatient BMT unit on 18-Jan-2019.

Subsequently the patient had multiple acute GvHD flares for which he was treated with ruxolitinib and budesonide. Stool cultures obtained on 04-Jun-2019 for symptoms of diarrhea and nausea were found to be positive for *C. difficile*. The patient had abdominal pain and electrolyte changes but no renal insufficiency at that time. The patient was started on vancomycin PO. The nausea, vomiting, and diarrhea improved in 24 hours. The *C. difficile* event was considered resolved on 07-Jun-2019.

Subject Identifier	GP3UMN-007
Age	53
Sex	Male
Baseline Weight (kg)	86.7
Race	White - North American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	11 Jan 2019
Event	1. Pneumonia 2. Pneumonia
Severity	1. Grade 2 2. Grade 2
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 12 Sep 2019 – 15 Sep 2019 2. 12 Dec 2019 – 13 Dec 2019
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	
Narrative: Patient GP3UMN-007 is a 53 year-old White, North American male with AML who received an Unmanipulated CBU transplant on 11-Jan-2019.	

The patient was diagnosed with AML on 01-Sep-2018. He underwent induction therapy with daunorubicin 60 mg/m^2 (02-Sep-2018 to 04-Sep-2018) and cytarabine 200 mg/m^2 (02-Sep-2018 to 07-Sep-2018), and consolidation therapy with HiDAC (10-Oct-2018 to 15-Oct-2018). The patient's past medical history included hyperlipidemia, heart murmur, bicuspid aortic valve disease with mild aortic stenosis, hypertension, anxiety, depression, vitamin D deficiency, gastroesophageal reflux disease, hemorrhoids, and *C. difficile* infection. He had moderate pulmonary impairment at study screening (FEV1 = 77% predicted). The patient surgical history included vasectomy (27-Jun-2018) and wedge resection (09-Nov-2018).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (07-Jan-2019 to 10-Jan-2019), fludarabine (03-Jan-2019 to 05-Jan-2019), and cyclophosphamide (03-Jan-2019 to 04-Jan-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included micafungin, acyclovir, trimethoprim-sulfamethoxazole, voriconazole, and levofloxacin. Neutrophil counts recovered at 18 days post-transplantation (29-Jan-2019). The patient was discharged from the hospital on 04-Feb-2020.

The patient was admitted to the inpatient unit on 12-Sep-2019 for fatigue and dyspnea. A chest CT on 12-Sep-2019 showed bibasilar pulmonary opacities. The patient's troponin was elevated at 1.056. EKG showed normal sinus rhythm. An echocardiogram was performed on 13-Sep-2019. The patient was diagnosed with pneumonia and treated with azithromycin (completed on 16-Sep-2019). The patient was discharged on 15-Sep-2019.

The patient then presented with shortness of breath on 12-Dec-2019. He reported recently vaping with tetrahydrocannabinol (THC). Pulmonary function testing on 10-Dec-2019 had shown abnormal findings for which he was referred to pulmonology. The patient was admitted to inpatient unit with new patchy reticulonodular infiltrates in the left lung base as well as ground-glass nodules in the right middle lobe. The patient was started on ceftriaxone and transitioned to azithromycin and albuterol inhaler as needed. Viral respiratory swabs were negative. The patient was discharged on 13-Dec-2019.

Subject Identifier	GP3UMN-008
Age	27
Sex	Female
Baseline Weight (Kg)	58.1
Race	White – North American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	18 Apr 2019
Event	No SAEs Reported
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	

Narrative:
Patient GP3UMN-008 is a 27 year-old White, North American female with AML who received an Unmanipulated CBU transplant on 18-Apr-2019. The patient was withdrawn from the study on 28-Mar-2019.

The patient was diagnosed with AML on 20-Nov-2018. She underwent induction therapy with one cycle of 7+3 with cytarabine and idarubicin starting on 01-Dec-2018. Reinduction therapy included one cycle of cladribine, cytarabine, mitoxantrone, and G-CSF (CLAG-M) starting on 20-Dec-2018. The patient's past medical history included anxiety, depression, attention-deficient hyperactivity disorder (ADHD), moderate/severe hepatic impairment, Herpes simplex infection, substance abuse (alcohol and marijuana), endometrioma, back pain, keratoconjunctivitis, and gastroesophageal reflux disease.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (14-Apr-2019 to 17-Apr-2019), fludarabine (10-Apr-2019 to 12-Apr-2019), and cyclophosphamide (10-Apr-2019 to 11-Apr-2019). Neutrophil counts recovered at 27 days post-transplantation (15-May-2019). The patient was discharged from the hospital on 15-May-2019. There were no SAEs reported post-transplantation.

Subject Identifier	GP3UMN-009
Age	45
Sex	Male
Baseline Weight (kg)	106.1
Race	White – North American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	13 Dec 2019
Event	No SAEs Reported
Severity	
Serious (Yes/no)	
Start/stop date of Event	
Outcome Of Event	
Relationship To The Study Drug	
Date Of Death (If Applicable)	
Narrative: Patient GP3UMN-009 is a 45 year-old White, North American male with AML who received an Unmanipulated CBU transplant on 13-Dec-2019. The patient was diagnosed with AML on 26-Sep-2019. He underwent induction therapy with 7+3 cytarabine and daunorubicin starting on 27-Sep-2019. The patient's past medical history included invasive fungal infection, sinus tachycardia, obesity, submandibular, juguodigastic, and proximal jugular lymph node enlargement (24-Sep-2019), gastritis (26-Sep-2019 to 19-Nov-2019), oral lesions (24-Sep-2019 to 22-Oct-2019), and hypothyroidism (14-Aug-2019). He had moderate pulmonary impairment (FEV1 = 73%) at study screening. The patient had reported allergies to shellfish derived products. Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of TBI (09-Dec-2019 to 12-Dec-2019), fludarabine (05-Dec-2019 to 07-Dec-2019), and cyclophosphamide (05-Dec-2019 to 06-Dec-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, levofloxacin, posaconazole, vancomycin, and valacyclovir. Neutrophil counts recovered at 29 days post-transplantation (12-Jan-2020). The patient was discharged from the hospital on 14-Jan-2020. There were no SAEs reported post-transplantation.	

Subject Identifier	GP3UTN-001
Age	58
Sex	Male
Baseline Weight (Kg)	78.0
Race	White – North American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	23 Aug 2019
Event	1. Mental Status Change 2. Acute Respiratory Failure
Severity	1. Grade 3 2. Grade 4
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 17 Sep 2019 – 09 Oct 2019 2. 21 Sep 2019 – 22 Sep 2019
Outcome Of Event	1. Resolved 2. Resolved
Relationship To The Study Drug	1. No 2. No
Date Of Death (If Applicable)	
Narrative:	

Patient GP3UTN-001 is a 58 year-old White, North American male with Myelodysplastic Syndrome who received an Unmanipulated CBU transplant on 23-Aug-2019.

The patient was diagnosed with Myelodysplastic Syndrome [refractory anemia with excess blasts (RAEB-2)] on 03-Dec-2018. He underwent induction therapy with six cycles of azacitidine (07-Jan-2019 to 14-Jun-2019). The patient's past medical history included HHV6 viremia, hypertension, coronary artery disease with stents (2003, 2013, and most recent stents on 02-May-2018), congestive heart failure (ejection fraction = 45%), dyslipidemia, and gastroesophageal reflux disease. He had moderate/severe pulmonary impairment at study screening. The patient's past surgical history included corneal transplant.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 90 mg/day (18-Aug-2019 to 20-Aug-2019), thiotepa 340 mg/day (16-Aug-2019 to 17-Aug-2019), and busulfan 222 mg/day (18-Aug-2019 to 20-Aug-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus [stopped on 17-Sep-2019 due to suspected posterior reversible encephalopathy syndrome (PRES)], cyclosporine (stopped on 18-Sep-2019 due to suspected PRES syndrome), and methylprednisolone 70 mg intravenous (IV) twice daily (15-Sep-2019). Infection prophylaxis included acyclovir, levofloxacin, micafungin, posaconazole, and vancomycin. The patient developed Herpes ophthalmitis and was treated with foscarnet since transplant. Neutrophil counts recovered at 26 days post-transplantation (18-Sep-2019). The patient was discharged from the hospital on 16-Oct-2019.

The patient developed mild confusion and lethargy on 14-Sep-2019 while still in the hospital for the transplant admission (16-Aug-2019 to 16-Oct-2019). A head CT was performed and did not detect any abnormalities. The patient then developed intermittent fever (max 39°F) on 16-Sep-2019 with persistent diarrhea. Stool workup was negative. The patient was diagnosed with acute GvHD symptoms with other possible etiologies including use of total parenteral nutrition (TPN) and engraftment syndrome.

The patient was found to have progressively worsening mental status with confusion on 17-Sep-2019. He did not follow commands on 19-Sep-2019 and only opened his eyes to noxious stimuli. The patient had multiple imaging studies done without any clear neurologic etiology revealed. electroencephalogram (EEG) showed an abnormal recording suggestive of mild generalized disturbance of cerebral function of non-specific etiology. No seizures or epileptiform abnormalities were recorded. The treating physician felt that right extremity weakness and mental status changes were attributable to PRES. The patient was treated empirically for viral encephalitis with intravenous (IV) foscarnet 60mg/kg every 12 hours. He was also on broad-spectrum antibiotics, anti-viral, and anti-fungal prophylaxis since transplant. He was given albumin, TPN, and aggressive IV fluid hydration for hypernatremia (146 mEq/L) and hyperglycemia (247 mg/dL).

Concurrent with the mental status changes, the patient developed acute respiratory distress, felt to be due to hyperacute GvHD and increased secretions. The patient was placed on BiPAP and noninvasive positive pressure ventilation (NIPPV) on 20-Sep-2019. Work of breathing improved with NIPPV. Right ventricular systolic pressure was monitored for respiratory distress since 17-Sep-2019. Arterial blood gases suggested respiratory alkalosis compensation (bicarbonate of 24 on 16-Sep-2019 and 21 on 18-Sep-2019, low CO_2 of 19 mmol/L, and high lactic acid of 2.2 mmol/L on 19-Sep-2019) and acute respiratory failure on 20-Sep-2019. The patient was transferred to the ICU on 21-Sep-2019 for intubation and was diagnosed with acute respiratory failure.

A CT scan of the chest on 20-Sep-2019 showed no infiltrates and no significant hypoxia. Bedside ultrasound on 20-Sep-2019 showed collapsed inferior vena cava, no evidence of pleural effusion/cardiac tamponade, hyperdynamic left ventricular function, no right ventricular strain, no B lines, and the presence of lung sliding. The patient was extubated on 22-Sep-2019 and transferred back to the BMT unit. He was on four liters of oxygen by nasal cannula, with oxygen saturations of 98-99%. On 22-Sep-2019, the patient's acute respiratory failure was considered resolved.

On 08-Oct-2019, the study clinician noted that the patient continued to have periods of mild confusion but was improving slowly. The patient was able to follow simple commands and was verbal. There was some right-sided weakness (lower extremity more than upper extremity). On 09-Oct-2019, the patient's mental confusion had resolved. The patient was alert and oriented to person, place, time, and situation.

Subject Identifier	GP3UTN-003
Age	56
Sex	Female
Baseline Weight (Kg)	104.5
Race	Black – African American
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	29 Oct 2019
Event	1. CMV Colitis 2. Chronic GvHD Flare 3. Pulmonary Embolus 4. Multifocal COVID Pneumonia
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 5
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 26 Dec 2019 – 12 Feb 2020 2. 26 May 2020 – 17 Oct 2020 3. 06 Jul 2020 – 13 Jul 2020 4. 25 Aug 2020 – 17 Oct 2020
Outcome Of Event	1. Resolved 2. Death 3. Resolved 4. Death
Relationship To The Study Drug	1. No 2. Yes 3. No 4. No
Date Of Death (If Applicable)	17 Oct 2020

Narrative:
Patient GP3UTN-003 is a 56 year-old Black, African American female with AML who received an Unmanipulated CBU transplant on 29-Oct-2019.

The patient was diagnosed with AML on 27-May-2019. She underwent induction therapy with FLAG starting on 29-May-2019. She also received two cycles of consolidation therapy with high-dose cytarabine (HiDAC) from 11-Jul-2019 to 19-Aug-2019. The patient's past medical history included Type II diabetes. She had moderate pulmonary impairment at study screening (DLCO = 79% on 18-Sep-2019).

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 100 mg/day (24-Oct-2019 to 26-Oct-2019), thiotepa 330 mg/day (22-Oct-2019 to 23-Oct-2019), and busulfan 240 mg/day (24-Oct-2019 to 26-Oct-2019). GvHD prophylaxis included mycophenolate mofetil and tacrolimus. Infection prophylaxis included acyclovir, posaconazole, and vancomycin. Neutrophil counts recovered at 22 days post-transplantation (20-Nov-2019). The patient was discharged from the hospital on 27-Nov-2019.

The patient was hospitalized for cytomegalovirus colitis from 26-Dec-2019 to 03-Feb-2020. The patient was then seen in the outpatient BMT clinic on 26-May-2020 for a follow-up visit. She reported fever at home with headache and fatigue. Labs were significant for critically low potassium (2.5 mEq/L) and magnesium (1.4 mg/dL) levels. She was admitted on 26-May-2020 for management of chronic GvHD flare, fever, fatigue, headache, and hypokalemia. The patient had reported GvHD symptoms of rash and GI symptoms as of the post-transplantation Day 35 assessment. On 28-May-2020, the patient was afebrile, electrolytes had corrected, and the headache had resolved. Diarrhea and fatigue persisted but improved. Treatment included

methylprednisolone being increased to 20 mg/day and the addition of mycophenolate 1 mg twice daily. The patient was discharged home on 29-May-2020 with instructions to return to the outpatient BMT clinic on 01-Jun-2020 for re-assessment. From the time of discharge through 08-Jul-2020, the chronic GvHD continued to wax and wane with upper and lower GI symptoms.

The patient was admitted on 06-Jul-2020 for syncope and recurrent electrolyte instability. She had three episodes of witnessed syncope over the prior half a year, with each incident lasting about 30 seconds to 1 minute. The most recent syncopal event occurred three days prior to admission after the patient had used the bathroom. She did not exhibit any post-ictal state upon awakening and reported shortness of breath at the time. The most recent transthoracic echocardiogram in Jan-2020 showed an ejection fraction of 65%. The patient was found to have a large right pulmonary embolus on CTA on 09-Jul-2020. Echo on 08-Jul-2002 showed no right heart strain. The patient was started on enoxaparin 80 mg twice daily. She was discharged on 13-Jul-2020.

On 03-Aug-2020, the GvHD was noted to be quiescent, and the patient continued treatment with prednisone, ruxolitinib (Jakafi), mycophenolate, and budesonide. The patient was then found to be COVID positive on 24-Aug-2020. She was afebrile but reported symptoms of malaise, non-productive cough, runny nose, and shortness of breath. Given her high-risk of progression due her co-morbid conditions the patient was admitted on 25-Aug-2020 for observation and therapy with remdesivir and convalescent plasma. The patient was discharged home in stable condition on 31-Aug-2020.

The patient presented on 01-Sep-2020 with low Grade temperature and oxygen saturation of 93% on room air. She reported that her previous symptoms including her cough had improved since discharge earlier in the week. A chest CT scan revealed multifocal pneumonia consistent with COVID-19 infection. She was re-hospitalized on 02-Sep-2020 for management of multifocal COVID pneumonia. The treatment plan included methylprednisolone, anti-coagulation for history of pulmonary embolism, and holding of mycophenolate. On 02-Sep-2020, the patient was afebrile with 100% oxygen saturation on room air. CRP was increased to 31 mg/L. A repeat plasma infusion (IVIG) was administered and the methylprednisolone continued. She was noted to have increased rhinorrhea but no change in cough. An immune reconstitution test showed that CD4 counts were down to 141 cells/mm3 and IgG level was below 200 mg/dL. Supportive care was continued and the pulmonary service followed the patient. A repeat COVID test was still positive. CT scans of the chest performed throughout the admission continued to show worsening pneumonia.

On 15-Oct-2020, the patient became septic with multi-organ failure. She was also noted to have moderate, extensive GvHD with skin hypo/hyperpigmentation, gut involvement, alopecia, and neuropathy. She was intubated but was unable to ventilate. She was placed on maximum doses of vasopressors and made DNR given her poor prognosis. She was also noted to have COVID-related hemophagocytic lymphohistiocytosis (HLH) for which she was treated with methylprednisolone, etoposide, and supportive transfusions. The patient died on 17-Oct-2020 due to multi-organ system failure related to COVID. Primary cause of death was noted as viral infection. Autopsy was not done.

Subject Identifier	GP3UTR-001
Age	18
Sex	Female
Baseline Weight (Kg)	50.0
Race	Black
Study Therapy	Omidubicel
Date Of Study Therapy Administration	16 Jan 2018
Event	1. Abdominal Infection 2. Respiratory Insufficiency 3. Adenovirus Reactivation 4. Suspected Airway Tract Infection 5. UTI/Pyelonephritis 6. Suspected Infection

	7. GvHD 8. Facialis Paresis 9. Significant Decrease Lung Function
Severity	1. Grade 3 2. Grade 4 3. Grade 3 4. Grade 3 5. Grade 4 6. Grade 2 7. Grade 3 8. Grade 1 9. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes 6. Yes 7. Yes 8. Yes 9. Yes
Start/stop date of Event	1. 10 Feb 2018 – 20 Feb 2018 2. 14 Feb 2018 – 17 Feb 2018 3. 26 Feb 2018 – 15 Mar 2018 4. 11 Mar 2018 – 22 Mar 2018 5. 09 Apr 2018 – 11 Apr 2018 6. 02 May 2019 – 03 May 2018 7. 05 May 2018 – 17 May 2018 8. 10 Jul 2018 – 20 Nov 2018 9. 30 Apr 2018 – 20 Nov 2018
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved with sequelae 4. Resolved 5. Resolved 6. Resolved 7. Resolved with sequelae 8. Resolved 9. Resolved
Relationship To The Study Drug	1. No 2. No 3. No 4. No 5. No 6. No 7. Yes 8. No 9. No
Date Of Death (If Applicable)	
Narrative: Patient GP3UTR-001 is an 18 year-old Black female with acute myeloid leukemia who received a Omidubicel transplant on 16-Jan-2018. The patient was diagnosed with acute myeloid leukemia without maturation (M1) on 20-Jun-2014. She received fludarabine, cytarabine, and granulocyte s factor (G-CSF) (FLAG) daunorubicin, fludarabine, ARA-	

C, and G-CSF. At relapse (19-Oct-2017) she received relapsed AML 2009 protocol (23-Oct-2017). Her past medical history included depression, anxiety, and thrombosis of the inferior vena cava and right iliac vein (treated with fraxiparine). She had a history of severe pulmonary dysfunction which required mechanical ventilation and invasive fungal infection which required IV antimicrobial treatment. She reported allergies to platelets, erythrocytes, and amphotericin B.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of thiotepa 270 mg/day (09-Jan-2018 to 10-Jan-2018), fludarabine 76.85 mg/day (11-Jan-2018 to 13-Jan-2018), and busulfan 207.90 mg/day (11-Jan-2018) and 240 mg/day (12-Jan-2018 to 13-Jan-2018). GvHD prophylaxis initially included mycophenolate mofetil and cyclosporine. Cyclosporine was then stopped due to liver toxicity and basiliximab plus prednisone was started. This regimen was then stopped, and tacrolimus was started. Infection prophylaxis included amphotericin B, ciprofloxacin, vancomycin, and ceftazidime. Neutrophil counts recovered at 10 days post-transplantation (26-Jan-2018). The patient was discharged from the hospital on 08-Feb-2018.

The patient was hospitalized for multiple infections (abdominal infection 10-Feb-2018, adenovirus reactivation 26-Feb-2018, suspected airway tract infection 11-Mar-2018, urinary tract infection (UTI)/pyelonephritis 09-Apr-2018, and other suspected infection 02-May-2018). The patient was admitted on 10-Feb-2018 due to fever, general malaise, and suspected enterocolitis and hemorrhagic cystitis. IV meropenem for 7 days was initiated for enterocolitis. Respiratory insufficiency was noted on 14-Feb-2018 with allo-lung imaging on 14-Feb-2018. Immune-mediated lung disease was suspected, differential diagnosis included GvHD and allo-lung syndrome. The patient was admitted to the ICU on 14-Feb-2018 for management of respiratory insufficiency and she was treated with steroid pulse (methyl prednisolone) and mechanical ventilation. At the time of transfer to the ICU the patient had severe dyspnea and hypoxia with low oxygen saturations. Despite ventilator support with oxygen mask and optiflow, antibiotics and steroids, her clinical condition deteriorated for which she was intubated and quickly started with high PEEP (25 cm H_2O). On intubation, hemorrhagic bronchus fluid appeared in large amounts. Hemorrhagic cystitis related to BK virus was treated with hyperhydration, oxybutynin, and tramadol. Hyperhydration was temporarily ceased due to massive pulmonary edema. Tacrolimus was stopped due to reduction in renal function.

On 16-Feb-2018, the patient had no more complications from the hyperhydration or bloody urine. She had produced substantial diuresis with >5 ml/kg/hour over the entire day, therefore Lasix was discontinued. Her tacrolimus was restarted. The patient was extubated on 16-Feb-2018. Bronchoalveolar lavage (BAL) was negative and no pathogens were found. Methylprednisolone was switched to prednisone on 17-Feb-2018. The patient was transferred from the ICU on 17-Feb-2018 but was continued on steroids. The patient had hypertension with pulse steroids, so she was started on amlodipine. Her neurology exam was slow, so she was started on Risperdal. The patient was continued on IV meropenem until 19-Feb-2018 when her antibiotics were stopped. A lung function test was initially extremely poor, however she showed improvement on a repeat lung function test on 07-Mar-2018 at which point the respiratory insufficiency event was considered resolved.

The patient was then admitted to the hospital on 05-May-2018 with stomach pain and vomiting which was later confirmed as GvHD. The patient had been previously diagnosed with mild gut GvHD (Grade II), confirmed by biopsy on 20-Apr-2018. Blood cultures and urine analysis were obtained. BK cystitis was found to be ongoing. IV meropenem for 7 days was initiated for suspected enterocolitis. Treatment with prednisone 2 mg/kg was started on 09-May-2018 and the patient recovered on prednisone. The GvHD event was reported as resolved on 17-May-2018.

Subject identifier	GP3UTR-002
Age	18
Sex	Female
Baseline weight (kg)	66.4
Race	White
Study therapy	Unmanipulated CBU
Date of study therapy administration	04 May 2018

Event	1. Gastrointestinal Blood Loss 2. Thrombotic Microangiopathy (TMA) 3. Rectal Bleeding/GvHD 4. Hypovolemic Shock 5. Respiratory Insufficiency 6. Acute Respiratory Distress Syndrome (ARDS) 7. Progressive Osteonecrosis 8. Hypotension
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 4 5. Grade 3 6. Grade 4 7. Grade 3 8. Grade 4
Serious (yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes 6. Yes 7. Yes 8. Yes
Start/stop date of Event	1. 30 May 2018 – 11 Jun 2018 2. 14 Jun 2018 – 31 Jan 2019 3. 01 Sep 2018 – 31 Jan 2019 4. 19 Oct 2018 – 19 Oct 2018 5. 23 Nov 2018 – 16 Jun 2019 6. 24 Dec 2018 – 07 Jan 2019 7. 13 Feb 2019 – 24 Jun 2019 8. 03 Jun 2019 – 06 Jun 2019
Outcome of event	1. Resolved 2. Resolved 3. Resolved 4. Resolved with sequelae 5. Resolved 6. Resolved with sequelae 7. Resolved 8. Resolved
Relationship to the study drug	1. No 2. No 3. Yes 4. No 5. No 6. No 7. No 8. No
Date of death (if applicable)	

Narrative:
Participant GP3UTR-002 is an 18 year-old White-European female with Acute Lymphoblastic Leukemia who received an unmanipulated cord blood unit transplant on 04-May-2018.

The participant was diagnosed with Acute Lymphoblastic Leukemia (Precursor B-Cell ALL) on 26-Jun-2017. She was treated according to Dutch Cancer Oncology Group (DCOG) ALL11 (HD-MTX, leucovorin,

MTX/ARA-C/DAF, IDA, FLU, and HD-ARA-C) and underwent 3 treatment courses (15-Jun-2017, 18-Dec-2017, and 26-Mar-2018). Her past medical history included invasive pulmonary fungal infection treated with amphotericin B, encephalopathy, renal insufficiency, and veno-occlusive disease (lung emboli). She had mild hepatic, severe pulmonary (FEV1 = 68% on 24-Apr-2018; FEV = 60% on 02-Mar-2018), and moderate/severe renal dysfunction at study screening.

Prior to unmanipulated cord blood unit transplant, the participant was treated with a myeloablative conditioning regimen consisting of fludarabine 93 mg/day (29-Apr-2018 to 01-May-2018), thiotepa 365 mg/day (27-Apr-2018 to 28-Apr-2018), and busulfan 246 - 360 mg/day (29-Apr-2018 to 01-May-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Neutrophil counts recovered at 16 days post-transplantation (20-May-2018). The participant was discharged from the hospital on 29-May-2018.

The participant was hospitalized for gastrointestinal hemorrhage from 30-May-2018 to 11-Jun-2018. She was then admitted on 14-Jun-2018 for management of nose bleeding and thrombocytopenia. The participant reported experiencing nose bleeds on a regular basis but had a severe nosebleed on 14-Jun-2018. There were attempts to manage the nosebleed with pressure and xylometazoline (Otirvin) spray, but it was not sufficient. The participant needed urgent thrombocyte transfusion on 15-Jun-2018 (Hb 6.1 mmol/L and thrombocytes 7x10^9/L). On 09-Jul-2018, the participant reported a slight amount of blood in her feces (Hb 5.4 mmol/L and thrombocytes 4x10^9/L). On 23-Jul-2017, she reported blood clots and fresh blood in her feces (Hb 5 mmol/L and thrombocytes 3x10^9/L). On 25-Jul-2018, she had another nosebleed which resolved after about 10 minutes. The participant had significant blood loss and she was managed with blood transfusions guided by clinical symptoms. The thrombocytopenia was reported as resolved as of 24-Aug-2018.

The participant was then admitted on 01-Sep-2018 for the management of GvHD. The participant presented with diarrhea and stomach pain. Infectious diagnostics were negative. The participant was diagnosed with GvHD on 06-Sep-2018 (03-Sep-2018 grade II gut, grade 0 skin, and grade 0 liver GvHD). Gastroduodenal and sigmoidoscopy on 06-Sep-2018 confirmed GvHD. She was started on steroids and was switched to sirolimus on 07-Sep-2018. The participant was then discharged on 02-Oct-2018. At discharge she had grade 1 gut, grade 0 skin, and grade 0 liver GvHD.

The participant was then readmitted from 11-Oct-2018 to 13-Oct-2018 for abdominal pain. The abdominal pain was associated with GvHD. She was readmitted again from 17-Oct-2018 to 18-Oct-2018 for back pain. The back pain was muscular and associated with muscle weakness due to steroid use. During the admission, the participant's pain medication was adjusted (diazepam added, paracetamol changed to 500mg). Then from 19-Oct-2018 to 24-Oct-2018, the participant was hospitalized for severe rectal bleeding. She was found to have a drop in hemoglobin (Hb 3.6 mol/L) and was managed for hypovolemic shock on 19-Oct-2018 (BP: 70/54, 97/63, 103/71, 93/62, 99/81, 98/80, 105/78, 121/81). An endoscopy on 20-Oct-2018 showed ulcerations and histology confirming GvHD. Treatment was intensified with prednisolone increased to 1.5 mg/kg, weekly basiliximab, and vedolizumab therapy. She was also treated with tranexaminic acid and daily thrombocyte transfusions to reduce bleeding risk.

The participant continued to have persistent therapy resistant GvHD. She was admitted locally from 11-Nov-2018 to 12-Nov-2018 for severe rectal bleeding with hemodynamic instability and transferred to the transplant center on 12-Nov-2019. Duodeno-colonoscopy done on 15-Nov-2018 showed findings supportive of thrombotic microangiopathy and mild GvHD. The participant was then hospitalized from 23-Nov-2018 to 26-Nov-2018. On 23-Nov-2018 she was transferred to the ICU for respiratory insufficiency. On 25-Nov-2018, she was transferred to the ICU for intestinal bleeding and approximately 1-liter blood loss. She received octreotide, novosen, and blood products.

The participant had a colonoscopy with biopsies performed on 30-Nov-2018 which showed extensive infectious ulcerations and fat necrosis supportive for thrombotic microangiopathy and mild GvHD. A CT angiogram performed on 04-Dev-2018 was negative and showed no clear cause for rectal bleeding. The participant was started on eculizumab (1x1200mg/w) on 19-Dec-2018. After receiving eculizumab therapy, the participant was no longer thrombocyte transfusion dependent.

On 24-Dec-2018, the participant presented with worsening respiratory distress. She had elevated CRP and fever. Chest x-ray showed Acute Respiratory Distress Syndrome. Pulmonary infection was suspected, and meropenem and vancomycin were started. On 28-Dec-2018, the participant was transferred to the ICU. She was intubated on 01-Jan-2019. Bronchoalveolar lavage was positive for adenovirus on 29-Dec-2018 and she was started on cidofovir. Blood tests were negative, so cidofovir was stopped again after 1 dose on 02-Jan-2018. The participant was extubated on 03-Jan-2019 but remained on optiflow (nasal cannula). Some pulmonary improvement was noted on 04-Jan-2019. The participant was transferred out of the ICU on 07-Jan-2019.

On 17-Jan-2019, the participant had some peaking fevers and a CRP of 250. On 31-Jan-2019 a repeat biopsy of the colon was done which showed no histology-based indication for the presence of TMA or GvHD (in contrast to the biopsy performed on 15-Nov-2018). The site reported TMA and GvHD to be resolved as of 31-Jan-2019, but the participant remained hospitalized for observation due to her poor general condition and complications (high CRP, frequent fever, pain, and respiratory insufficiency). The participant was then diagnosed with progressive osteonecrosis on 13-Feb-2019.

The participant's blood pressure dropped to 59/21 mm HG on 03-Jun-2019. The participant was not responding to fluid boluses and hydrocortisone. There was no history of fever, but there was an increase in CRP. The participant was transferred to the ICU on 03-Jun-2019 for management of hypotension. Meropenem and vancomycin were started for suspected sepsis on 04-Jun-2019. Metabolic acidosis was treated with bicarbonate supplementation. Echocardiography on 04-Jun-2019 showed decreased function (differential diagnosis: acute sepsis or cardiotoxicities). The participant was discharged from the ICU on 06-Jun-2019. Meropenem and vancomycin were stopped, and prophylaxis regimen was restarted. Blood cultures were negative, but the working diagnosis for the hypotension event was sepsis.

Participant developed suspected pulmonary aspergillosis according to a thoracic CT scan performed on 23-Mar-2021. On 26-Mar-2021 (day +1057), there was suspicion for donor-derived secondary AML but due to the participant's severe dyspnea, a bone marrow exam was not possible. The participant died on 26-Mar-2021 due to suspected pulmonary aspergillosis. An autopsy was not done but chimerisms performed on residual material post-mortem revealed 100% donor cells.

Subject Identifier	GP3UVA-001
Age	47
Sex	Male
Baseline Weight (Kg)	92.5
Race	White
Study Therapy	Omidubicel
Date Of Study Therapy Administration	12 Feb 2020
Event	1. Febrile Neutropenia 2. Neutropenic Fever 3. Mucositis 4. Laryngeal Edema 5. Febrile Neutropenia
Severity	1. Grade 3 2. Grade 3 3. Grade 4 4. Grade 3 5. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes 5. Yes
Start/stop date of Event	1. 18 Nov 2019 – 22 Nov 2019

	2. 16 Dec 2019 – 21 Dec 2019 3. 12 Feb 2020 – 25 Mar 2020 4. 13 Feb 2020 – 23 Feb 2020 5. 12 Feb 2020 – 10 Mar 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved 4. Resolved 5. Resolved
Relationship To The Study Drug	1. NA: Pre-transplant Event 2. NA: Pre-transplant Event 3. No 4. No 5. No
Date Of Death (If Applicable)	

Narrative:

Patient GP3UVA-001 is a 47 year-old White male with Acute Myelomonocytic Leukemia who received a Omidubicel transplant on 12-Feb-2020.

The patient was diagnosed with Acute Myelomonocytic Leukemia (M4) on 19-Sep-2019. Induction therapy was initiated on 20-Sep-2019 with 7+3 and midostaurin. Consolidation therapy with high-dose cytarabine began on 29-Oct-2019 with the addition of intrathecal cytarabine. Cycle two of consolidation was given on 26-Nov-2019. No significant medical history or allergies were reported at study screening.

The patient was admitted to an outside facility on 18-Nov-2019 for management of febrile neutropenia. His ANC at the time was 0.2 x 10^9/L and he presented with a fever of 38.9^{o}C. The patient reported fever, chills, body aches, and swollen lymph nodes. He denied shortness of breath, pain, and vomiting. The patient was treated with cefepime and vancomycin. He was discharged on 22-Nov-2019 on levofloxacin. The patient was readmitted to an outside facility on 16-Dec-2019. He presented with fever, neutropenia, and anemia. He had no other signs of infection. The patient was treated with cefepime. Blood cultures remained negative. Neutrophil counts increased to 0.9 x 10^9/L on 21-Dec-2019. He was discharged on 21-Dec-2019 on oral levofloxacin to be taken daily for seven days.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of thiotepa 411 mg/day (01-Feb-2020 to 02-Feb-2020), TBI 150 cGy (03-Feb-2020 to 06-Feb-2020), and fludarabine 82 mg/day (07-Feb-2020 to 10-Feb-2020). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included posaconazole, acyclovir, and pentamidine. Neutrophil counts recovered at 25 days post-transplantation (08-Mar-2020). The patient was discharged from the hospital on 18-Mar-2020.

Prior to receiving the transplant, the patient reported dysphagia and odynophagia on 09-Feb-2020 that the treating team felt was related to TBI. The pain was managed with as needed oral pain medication. On 12-Feb-2020 the patient was pretreated with hydrocortisone per protocol and received his transplant as planned. The dysphagia and odynophagia improved briefly after the transplant but then worsened again. The patient developed a fever the evening of the transplant and blood cultures were obtained. The patient was treated empirically with cefepime and vancomycin. Infectious workup with urinalysis and a chest X-ray were both unrevealing.

The odynophagia worsened over the course of the night, and by the early morning the patient was unable to tolerate his own secretions and had progressive dyspnea and stridor at rest. The patient was evaluated by ENT the morning of 13-Feb-2020. A laryngoscopy exam showed severe laryngeal edema thought to be related to mucositis. The patient was given an intravenous dose of methylprednisolone. Given concern for imminent airway compromise, the intensive care team evaluated the patient, and he was transferred to the medical intensive care unit (MICU) for acutely worsening odynophagia and dysphagia. Dexamethasone, diphenhydramine, and racemic epinephrine were administered. One hour after the steroid dose, ENT re-scoped the patient and found the laryngeal edema to be minimally improved.

On re-evaluation four hours after steroid administration, the patient felt markedly improved and was tolerant of his own secretions. Consulting teams agreed that the timing of the edema was inconsistent with an allergic reaction to the transfusion. The patient continued to improve and one day after transfer to the MICU felt back to his baseline of mild odynophagia. The patient was able to tolerate fluids, medications, and food by mouth. ENT cleared the patient to return to the BMT service on 16-Feb-2020. The laryngeal edema event was reported as resolved as of 23-Feb-2020.

Upon exam on 24-Mar-2020, the provider noted the presence of oropharyngeal exudate, but the next day the oropharynx was assessed as clear with normal mucous membranes and no oropharyngeal exudate. The site has deemed this event as resolved, with no residual effects.

Subject Identifier	GP3VAL-002
Age	53
Sex	Male
Baseline Weight (Kg)	94.1
Race	Caucasian
Study Therapy	Omidubicel
Date Of Study Therapy Administration	22 Aug 2017
Event	1. GvHD 2. Thrombotic Microangiopathy
Severity	1. Grade 3 2. Grade 5
Serious (Yes/no)	1. Yes 2. Yes
Start/stop date of Event	1. 07 Sep 2017 – 05 Oct 2017 2. 02 Nov 2017 – 23 Nov 2017
Outcome Of Event	1. Resolved 2. Death
Relationship To The Study Drug	1. Yes 2. No
Date Of Death (If Applicable)	23 Nov 2017

Narrative:
Patient GP3VAL-002 is a 53 year-old Caucasian male with ALL who received a Omidubicel transplant on 22-Aug-2017.

The patient was diagnosed with ALL (Philadelphia chromosome positive) on 10-Jan-2017. Treatment was started with imatinib 600 mg/24h. Once the pre-phase treatment was completed (7 days), and with a definitive diagnosis of mature B cell phenotype Ph+ ALL, treatment was started according to PETHEMA protocol LAL-PH08 (Day 1 of the protocol on 16-Jan-2017). In the presence of complete cytologic remission, the first consolidation cycle was initiated with protocol LAL-PH08 (day 1 of the protocol on 23-Mar-2017). The last cycle was in June 2017 with high-dose methotrexate and IT therapy. The patient had complete molecular remission after treatment in accordance with PETHEMA. The patient's additional medical history included hypertension, dyslipidemia, obesity, Gilbert syndrome, liver steatosis, and heart valve disease.

Prior to Omidubicel transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 91.6 mg/day (17-Aug-2017 to 19-Aug-2017), thiotepa 360 mg/day (15-Aug-2017 to 16-Aug-2017), and busulfan 230.4 mg/day (17-Aug-2017 to 19-Aug-2017). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Other medications included pantoprazole, fluconazole, metoclopramide, lorazepam, ondansetron, amphotericin B, fluconazole, amphotericin B, dexketoprofen, magnesium sulfate acyclovir, morphine, lorazepam, budesonide, amlodipine, enalapril, and

methylprednisolone. He received pentamidine inhalation on 16-Aug-2017. Neutrophil counts recovered at 7 days post-transplantation (29-Aug-2017). The patient was discharged from the hospital on 05-Oct-2017.

The patient was admitted to the hospital on 07-Sep-2017 with a history of vomiting, diarrhea, and abdominal pain. Given a suspicion of acute intestinal GvHD, a biopsy was performed and oral budesonide was initiated on 15-Sep-2017. While awaiting biopsy results, and with persistent symptoms, the decision was made to start systemic corticosteroids at a dose of 1 mg / kg on 18-Sep-2017. Lower GI GvHD was confirmed by rectal biopsy. The patient then reported a decrease in bowel movement volume but had persistent abdominal pain after ingesting food. A digestive colonoscopy and an abdominal CT were performed. Radiological results indicated resolving acute cholecystitis and the patient was referred to surgery for evaluation. The patient was discharged on 05-Oct-2017. The event was reported as resolved as of 05-Oct-2017, although treatment for GvHD continued.

The patient was then admitted on 02-Nov-2017 with thrombotic microangiopathy. Thrombotic microangiopathy was initially suspected on 17-Oct-2017 at which point the patient's cyclosporine was stopped. The patient was admitted to the hospital on 02-Nov-2017 with a three-week history of slow thinking, anhedonia, and abulia which did not improve after starting antidepressant treatment and evaluation by psychiatry. The patient had persistent nausea, hyporexia, and low food intake. There were no signs of acute neurological foci. The medical team suspected thrombotic microangiopathy, so plasma exchanges were started on 07-Nov-2017.

As of 17-Nov-2017, the patient was continuing with plasma exchanges for thrombotic microangiopathy. On 23-Nov-2017, the patient had worsening of his neurologic and respiratory functions because of thrombotic microangiopathy. The plasma exchanges and additional tests that were pending were stopped. The patient was calm and did not report any pain. A minimal dose of continuous perfusion morphine was started to relieve respiratory distress. The patient died on 23-Nov-2017. Autopsy was not performed. The hospital discharge summary noted cause of death as immediate cause: Respiratory insufficiency; Intermediate cause: Thrombotic microangiopathy; Fundamental cause: ALL. The site investigator considered thrombotic microangiopathy as the primary cause of death and the site did not report any secondary causes of death.

Subject Identifier	GP3VAL-004
Age	27
Sex	Female
Baseline Weight (Kg)	95.2
Race	White
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	18 Jul 2018
Event	1. Parainfluenza Infection/CMV Reactivation 2. GvHD 3. Fever 4. GvHD
Severity	1. Grade 3 2. Grade 3 3. Grade 3 4. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes 4. Yes
Start/stop date of Event	1. 10 Aug 2018 – 21 Sep 2018 2. 23 Sep 2018 – 23 Jan 2019 3. 13 Feb 2019 - 15 Feb 2019 4. 18 Feb 2019- 21 Aug 2019
Outcome Of Event	1. Resolved

	2. Resolved 3. Resolved 4. Resolved
Relationship To The Study Drug	1. No 2. Yes 3. No 4. Yes
Date Of Death (If Applicable)	

Narrative:
Patient GP3VAL-004 is a 27 year-old White female with acute myelogenous leukemia (AML) who received an Unmanipulated CBU transplant on 18-Jul-2018.

The patient was diagnosed with AML (with 11q23 [MLL] abnormalities) on 20-Mar-2018. The patient underwent induction therapy with idarubicin 12 mg/d and cytarabine 200 mg/m^2 (3+7 regimen) and consolidation therapy with high-dose cytarabine (completed on 26-May-2018). The patient's past medical history also included obesity. CMV was positive at screening.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine 94 mg/day (13-Jul-2018 to 15-Jul-2018), thiotepa 391 mg/day (11-Jul-2018 to 12-Jul-2018), and busulfan 250 mg/day (13-Jul-2018 to 15-Jul-2018). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included ciprofloxacin, amphotericin B, fluconazole, acyclovir, and posaconazole. Neutrophil counts recovered at 17 days post-transplantation (04-Aug-2018). The patient was discharged from the hospital on 08-Aug-2018.

The patient was admitted for cytomegalovirus infection from 10-Aug-2018 to 21-Sep-2018. The patient was then admitted to the hospital on 23-Sep-2018 with fever, nausea, vomiting, diarrhea, and impaired performance status. Pathology reports from gut and stomach biopsies were suggestive of graft-versu- host disease and cytomegalovirus disease. The patient was started on prednisone, letermovir (ganciclovir and foscarnet could not be administered because of toxicity), and total parenteral nutrition. The patient was able to be discharged home on 23-Jan-2019 after symptom improvement. The GvHD event was considered resolved on 23-Jan-2019 and the site determined the patient recovered with no residual effects.

The patient was then admitted for pyrexia from 13-Feb-2019 to 15-Feb-2019. On 18-Feb-2019 the patient was again hospitalized for the management of GvHD. The patient was admitted on 18-Feb-2019 because of undernourishment, nausea, vomiting, diarrhea, and abdominal pain. On 21-Feb-2019, an endoscopy with biopsy was done which confirmed intestinal GvHD. Immunosuppressive therapy was intensified with the addition of rapamycin, ibrutinib (at a dose of 420 mg/day), increased corticosteroids (2 mg/kg), and photopheresis sessions given weekly.

Secondary to severe intestinal GvHD and oral intolerance, the patient had severe malnutrition with hypoglycemia of 1.9 g/dL, and parenteral nutrition was initiated. She had severe abdominal pain which was difficult to control and required 23 rescues of transmucosal fentanyl. As a complication of the high-dose of analgesia with opioids she developed paralytic ileus, exacerbating the symptoms of emesis and abdominal pain. The ileus resolved after a period of no oral intake, nasogastric tube feeds, and modification to the analgesics.

The GvHD hospitalization was complicated by *Pseudomonas* bacteremia with cutaneous seeding in the form of disseminated subcutaneous nodules (confirmed *Pseudomonas* in a punch biopsy). The bacteremia was treated with ceftazidime for 14 days with clinical resolution. She had hypoalbuminemia with peripheral edema so parenteral albumin replacement was initiated. As ibrutinib causes hematologic toxicity with worsening of cytopenias (anemia and thrombocytopenia) as well as skin diathesis, her dose was lowered to 280 mg/day.

The patient continued to have complications including multiple ileal stenoses. She required surgery on 30-Apr-2019, including an ileal resection with anastomosis, due to several strictures. On 10-May-2019, the patient underwent a resection of the small intestine and ileostomy for peritonitis secondary to suture dehiscence. Culture of abdominal fluid was positive for *Enterococcus faecalis* and antibiotic therapy with ertapenem and

teicoplanin was initiated. The patient was stable for discharge on 05-Jun-2019 and continued home administration of antibiotics. The patient continued to be monitored and on 25-Jun-2019 a CT scan of the abdomen showed a reduction in the size of pelvic intra-abdominal collections compared to previous exams. Location of fluid collections made draining impossible. The patient was then found to have CMV reactivation on 01-Jul-2019 and valganciclovir was started. Antibiotic treatment was completed on 02-Jul-2019.

On 04-Jul-2019, the patient presented to the emergency department with complaints of abdominal pain, distension, and vomiting. There was concern for an intestinal blockage. A CT scan of the abdomen was performed on 07-Jul-2019 which showed a decrease in the collection adjacent to the rectum, a decrease in the collection in the abdominal wall, and the disappearance of the collection adjacent to the stoma. The CT also showed the appearance of wall thickening in handles of the small intestine with infiltration of the adjacent fat and an increase in peripancreatic fluid. A colonoscopy with biopsies was performed to rule out the presence of intestinal GvHD. The patient improved and was deemed stable for discharge home on 21-Aug-2019. The site considered the GvHD event to be resolved with no residual effects on 21-Aug-2019.

Subject Identifier	GP3VAL-005
Age	20
Sex	Male
Baseline Weight (Kg)	91.0
Race	White - Mediterranean
Study Therapy	Unmanipulated CBU
Date Of Study Therapy Administration	03 Dec 2019
Event	1. Pneumonia 2. Sinusoidal Occlusive Syndrome 3. Pleural Effusion
Severity	1. Grade 3 2. Grade 3 3. Grade 3
Serious (Yes/no)	1. Yes 2. Yes 3. Yes
Start/stop date of Event	1. 11 Dec 2019 – 01 Jan 2020 2. 10 Dec 2019 – 02 Jan 2020 3. 30 Jan 2020 – 06 Feb 2020
Outcome Of Event	1. Resolved 2. Resolved 3. Resolved
Relationship To The Study Drug	1. No 2. No 3. No
Date Of Death (If Applicable)	

Narrative:
Patient GP3VAL-005 is a 20 year-old White, Mediterranean male with ALL who received an unmanipulated CBU transplant on 03-Dec-2019.

The patient was diagnosed with ALL on 25-Jun-2017. He underwent induction therapy with PETHEMA protocol (daunorubicin, vincristine, asparaginase, and prednisone) plus TIT (methotrexate, cytarabine, and hydrocortisone) starting on 27-Jun-2017. Consolidation therapy included course 1 with methotrexate, vincristine, asparaginase, and dexamethasone (31-Aug-2017), course 2 with dexamethasone, cytarabine, asparaginase, and TIT (methotrexate, cytarabine and hydrocortisone) (22-Sep-2020), course 3 with asparaginase (25-Oct-2017), and a course with Erwinia (30-Nov-2017). Maintenance therapy included mercaptopurine 100 mg/day (21-Feb-2019 to 15-Jul-2019) and reinduction therapy included one cycle of inotuzumab (10-Sep-2019 to 25-Sep-2019). The patient's past medical history included acute appendicitis and peritonitis (Oct-2016), minor beta thalassemia, and Grade 1 fat gynecomastia. He had a history of infections

with *B. cereus*, *Pseudomonas*, and *Klebsiella pneumoniae*. The patient's surgical history included an appendectomy on 28-Oct-2016.

Prior to Unmanipulated CBU transplant, the patient was treated with a myeloablative conditioning regimen consisting of fludarabine (28-Nov-2019 to 30-Nov-2019), thiotepa (26-Nov-2019 to 27-Nov-2019), and busulfan (28-Nov-2019 to 30-Nov-2019). GvHD prophylaxis included mycophenolate mofetil and cyclosporine. Infection prophylaxis included acyclovir, pentamidine, micafungin, amphotericin B, fluconazole, and voriconazole. Neutrophil counts recovered at 26 days post-transplantation (29-Dec-2019). The patient was discharged from the hospital on 17-Jan-2020.

The patient was started on prophylactic defibrotide at the start of the transplant process given the patient's high-risk for hepatic veno-occlusive disease (previous treatment with inotuzumab and advanced disease). The patient started gaining weight gain and had increased abdominal girth on 10-Dec-2019 (85 kg, 98 cm on 10-Dec-2019 and 93.5 kg, 105 cm on 16-Dec-2019). He also had painful hepatomegaly and blood tests showed a progressive increase in bilirubin (maximum level of 1.5 mg/dL on 17-Dec-2019). The patient was diagnosed with sinusoidal occlusive syndrome and was started on supportive treatment with furosemide and ursodeoxycholic acid. He was continued on defibrotide.

The patient began having neutropenic fevers on 11-Dec-2019 (post-transplantation day +7). Chest X-ray showed a pneumonia in the upper right lobe. CT confirmed the pneumonia and showed condensation in the anterior segment of the upper right lobe. The patient was started on treatment with broad-spectrum antibiotics (meropenem and a single dose of amikacin) and supportive oxygen therapy. The patient deteriorated and required increasing oxygen flow. An additional CT scan showed progression of the pneumonia and bilateral pleural effusion. Anti-fungal treatment with teicoplanin was started and furosemide was added. The pneumonia was considered resolved on 01-Jan-2020. The sinusoidal occlusive disease was then considered resolved on 02-Jan-2020.

On 29-Jan-2020 a CT scan showed improvement in parenchymal involvement but a slight increase in pleural effusion. Pleural fluid was then drained. On 30-Jan-2020 the patient was admitted, and several diagnostic and evacuating thoracenteses were performed on the right pleural effusion. Hemothorax and infiltration by AML were ruled out. The patient was afebrile and stable on 05-Feb-2020. He was discharged home on 06-Feb-2020.

14.3.2 Abnormal Laboratory Value Listing

Individual laboratory values are presented in Listing 16.2.8. Abnormal laboratory values were observed in all patients and are discussed in Section 12.3.

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16 APPENDICES

16.1 Study Information

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16.1.1 Protocol and Protocol Amendments

The protocol and protocol amendments are presented in Appendix 16.1.1.

16.1.2 Sample Case Report Forms

The sample Case Report Forms are presented in Appendix 16.1.2.

16.1.3 List of IECs and/or IRBs

The list of IECs and IRBs is presented below. Additional representative written information for patient and sample consent forms is presented in Appendix 16.1.3.

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
USA	CAL01	University of California at Los Angeles	UCLA Office of the Human Research Protection Program	10889 Wilshire Blvd, Suite 830, Los Angeles, CA 90095	310-825-7122	00004642
USA	CCF01	Cleveland Clinic	Cleveland Clinic Foundation Institutional Review Board	9500 Euclid Avenue, Cleveland, Ohio 44195	216-444-2924	00005367
USA	CHC01	City of Hope Comprehensive Cancer Center Adults	Western Institutional Review Board (WIRB)	1019 39th Ave SE/Suite 120, Puyallup WA 98374	800-562-4789	N/A Central IRB do not have FWAs
USA	CHP01	Children's Hospital of Pittsburgh	Western Institutional Review Board (WIRB)	1019 39th Ave SE/Suite 120, Puyallup WA 98374	800-562-4789	N/A Central IRB do not have FWAs
USA	CMC01	Children's Medical Center of Dallas	UT Southwestern Medical Center IRB	5323 Harry Hines Blvd, Dallas, TX 75390	214-648-3060	00005087
USA	DCH01	Denver Children's Hospital	Colorado Multiple Institutional Review Board	University of Colorado, Anschutz Medical Campus 13001 E. 17th Place. Building 500, Room N3214, Aurora, CO, 80045	303-724-1055	00005070
USA	DFC01-BCH01	Dana Farber Cancer Institute	Dana-Farber Cancer Institute Office of Human Research Studies	450 Brookline Ave, OS229, Boston, MA 02215	617-632-3029	00001121
USA	DUK01-DUP01	Duke University Medical Center Adults	DUHS Institutional Review Board	2424 Erwin Rd, Suite 405, Durham, NC 27705	919-668-5111	00009025
USA	HFM01	Henry Ford Medical Center	Henry Ford Health System, Research Administration	1 Ford Place - 2F, Detriot, MI, 48202	313-874-4464	00005846
USA	KMC01	Kansas Medical Center	University of Kansas Medical Center Human Research Protection Program	Mail Stop 1032, 3901 Rainbow Blvd., Kansas City, KS, 66160	913-588-1240	00018719

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
USA	LOY01	Loyola University Medical Center	Institutional Review Board for the Protection of Human Subjects, Loyola University Chicago - Health Sciences Division	2160 South First Ave., Maywood, IL 60153	708-216-4608	00017487
USA	MCC01	Moores Cancer Center	University of California, San Diego, Human Research Protections Program	9500 Gilman Drive, Mail code 0052, La Jolla, California, 92093	858-246-4777	00004495
USA	NWU01	Northwestern University	Northwestern University Institutional Review Board, Biomedical IRB	750 N. Lake Shore Dr., 7th FL, Chicago, Il 60611	312-503-9338	00001549
USA	OHS01	Oregon Health and Science University	OHSU Institutional Review Board	3181 SW Sam Jackson Park Rd – L106RI, Portland, OR 97239	503-494-7887	00000161
USA	RCI01	Rutgers Cancer Institute of New Jersey	Western Institutional Review Board (WIRB)	1019 39th Ave SE/Suite 120, Puyallup WA 98374	800-562-4789	N/A Central IRB do not have FWAs
USA	SCI01	Standford University Cancer Institute	Administrative Panels on Human Subjects in Medical Research (IRB)	1705 El Camino Real, Palo Alto, CA 94306	650-723-2480	00000935
USA	UMD01	University of Maryland	University of Maryland, Baltimore Institutional Review Board	620 W. Lexington St. Second Floor, Baltimore MD 21201	410-706-5037	00007145
USA	UMN01	University of Minnesota	University of Minnesota Human Research Protection Program	Room 350-2 McNamara Alumni Center, 200 Oak Street SE Minneapolis, MN 55455	612-626-5654	00000312
USA	UTN01	University of Tennessee Cancer Institute	The University of Tennessee Health Science Center	910 Madison Ave, Suite 600, Memphis, TN, 38163	901-448-4824	00002301
USA	UVA01	University of Virginia	IRB for Health Sciences Research University of Virginia	PO Box 800483, Charlottesville, VA, 22903	434-924-9634	00006183
BRA	Brazil (country regulatory authority)	N/A	N/A for Brazil	N/A for Brazil	N/A for Brazil	N/A

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
BRA	CSA01	Hospital do Câncer de São Paulo Adults	Comissão de Ética para Análise de Projetos de Pesquisa - CAPPesq	Rua Dr. Ovídio Pires de Campos, 225, 5º andar do Prédio da Administração, Cerqueira César, São Paulo – SP - CEP: 05403-010 Email: cappesq.adm@hc.fm.usp.br	(11) 2661-7585, 2661-1548 e 2661-1549	N/A
BRA	CSP01	Hospital do Câncer de São Paulo Pediatrics	Comissão de Ética para Análise de Projetos de Pesquisa - CAPPesq	Rua Dr. Ovídio Pires de Campos, 225, 5º andar do Prédio Administrativo, Cerqueira César, São Paulo – SP - CEP: 05403-010 Email: cappesq.adm@hc.fm.usp.br	11) 2661-7585, 2661-1548 e 2661-1549	N/A
BRA	IAE01	Israelita Albert Einstein Hospital	Comitê de Ética em Pesquisa do Hospital Israelita Albert Einstein	Avenida Albert Einstein, 627/701 Morumbi – São Paulo-SP - 2ss bloco A - CEP: 05652-900 Email: cep@einstein.br	(11) 2151-3729	N/A
BRA	INC01	Instituto Nacional de Câncer José Alencar Gomes da Silva	Comitê de Ética em Pesquisa do Instituto Nacional de Câncer José Alencar Gomes da Silva - INCA	Rua do Resende, 128 - sala 203 - Centro - Rio de Janeiro - CEP: 20230-130 Email: cep@inca.gov.br	(21) 3207-4550 e 3207-4556	N/A
BRA	RPM01	Ribeirao Preto Medical Center	Comitê de Ética do Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da USP - HCFMRP/USP	Hospital das Clinicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo - Campus Universitário s/n - Subsolol - Monte Alegre - Ribeirão Preto - CEP: 14048-900 Email: cep@hcrp.usp.br	(16) 3602-2228	N/A
ESP	Spain (country regulatory authority)	N/A	Comité de Ética de la Investigación con medicamentos - CEIm La Fe	Avinguda de Fernando Abril Martorell, 106, 46026 València, Valencia, SPAIN	+34 961 24 40 00	N/A
ESP	BEL01	Institut Català d'Oncologia (ICO) Bellvitge	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
ESP	HSP01	Hospital Sant Pau	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
ESP	JDD01	Hospital Sant Joan de Deu	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
ESP	LAF01	Hospital Universitario La Fe	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
ESP	LAP01	Hospital Universitario La Fe Pediatrics	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
ESP	VAL01	Universitary Hospital Vall d'Hebron	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
ESP	VAP01	Universitary Hospital Vall d'Hebron Pediatrics	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
ESP	VDR01	Hospital Universitario Virgen del Rocío	N/A, in Spain, the study is evaluated by one sigle IRB that acts as country IRB.	N/A	N/A	N/A
FRA	France (country regulatory authority)	N/A	Comité de Protection des Personnes (CPP) Sud-Ouest et Outre-mer II ARS Midi Pyrénées	10 chemin du raisin 31050 TOULOUSE Cedex 9 France Cppsoom2@ars.sante.fr	05.34.30.27.56 Fax : 05.34.30.27.38	N/A
FRA	DEB01	Hospital Robert-Debre	N/A only country EC	N/A only country EC	N/A only country EC	N/A
GBR	UK (country regulatory authority)	N/A	SOUTH CENTRAL – OXFORD A	North End (Lecture Theatre) OCDEM Building - Churchill Hospital OX3 7 LE - United Kingdom	0207 104 8048	N/A
GBR	MAN01	Manchester University Hospital	Research Office Manchester University NHS Foundation Trust	1st floor, The Nowgen Centre 29 Grafton Street, Manchester, M13 9WU	+44(0)161 276 3565	N/A

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
GBR	QEH01	Queen Elizabeth Hospital Center for Clinical Hematology	UHB NHS Foudation trust Research and Innovation	First Floor West, ITM Building, Heritage Building, Queen Elizabeth Hospital, Mindolsohn Way, Edgbaston, Birmingham, B15 2TH	(+44) 0121 371 4185	N/A
GBR	RMH01	The Royal Marsden Hospital	The Royal Marsden's Haemato-oncology Unit	The Royal Marsden Fulham Road, London SW3 6JJ	Tel: (+44) 020 7352 8171	N/A
GBR	SJU01	St. James's University Hospital	Research And Innovation Centre	Beckett St, Leeds LS9 7TF St James's University Hospital	(+44) 0113 206 0478	N/A
ITA	Italy (country regulatory authority)	N/A	N/A for Italy	N/A for Italy	N/A for Italy	N/A
ITA	CAR01	Careggi University Hospital	Comitato Etico Area Vasta Centro	Azienda Ospedaliero-Universitaria Careggi Largo Brambilla, 3 - 50134 Firenze segrcesf@unifi.it	0039 055 794 6999	N/A
ITA	OBG01	Ospedale Pediatrico Bambino Gesù of Rome	Comitato Etico dell'IRCCS Ospedale Pediatrico Bambino Gesù	OPBG - Viale di Villa Pamphili 100 - 00152 Roma comitato.etico@opbg.net	0039 06 6859 3580	N/A
NLD	The Netherlands (country regulatory authority)	N/A	Centrale Comissie Mensgebonden Onderzoek (CCMO)	Centrale Commissie Mensgebonden Onderzoek (CCMO) Postbus 16302, 2500 BH Den Haag	+31 (0) 70 340 6700	N/A
NLD	PMC01	Prinses Maxima Children's Hospital	N/A only country EC	N/A only country EC	N/A only country EC	N/A
NLD	UTR01	Utrecht University	N/A only country EC	N/A only country EC	N/A only country EC	N/A

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
PRT	Portugal (country regulatory authority)	N/A	Comissão de Ética para a Investigação clínica	CEIC - Parque da Saúde de Lisboa Av. do Brasil, 53 - Pav. 17-A, 1749-004 Lisboa ceic@ceic.pt	+351 21 798 53 40 Fax: +351 21 798 71 05	N/A
PRT	IPO01	Instituto Português de Oncologia Francisco Gentil	Conselho de Administração do Instituto Portugues de Oncología de Lisboa Francisco Gentil, E.P.E	Unidade de Investigação Clínica – Pavilhão Central – 1º andar Rua Professor Lima Basto 1099-023 Lisboa Portuga	+351 217229800 /Ext. 1106	N/A
SGP	Singapore (country regulatory authority)	N/A	Singapore Centralised Institutional Review Board	168 Jalan Bukit Merah #06-08 Tower 3, Connection One, Singapore 150168	Tel: +65-6323 7517	N/A
SGP	NUH01	National University Hospital	N/A only country EC	N/A only country EC	N/A only country EC	N/A
SGP	SGH01	Singapore General Hospital	N/A only country EC	N/A only country EC	N/A only country EC	N/A
ISR	Israel (country regulatory authority)	N/A	Israeli Ministry of Health (MoH)	The Clinical Trials Department - Medical Devices and Advanced Therapies The Ministry Of Health, P.O.B 1176, Jerusalem 9101002 Capital Towers No. 2, Floor 2, Rooms 237 + 239	5400 08-6241010	N/A
ISR	HAD01	Hadassah Medical Center	The Institutional Helsinki Committee Hadassah Medical Organization	Kiryat Hadassah, The 'Old' Building, Floor 5 Ein Kerem Hospital, Hadassah Medical Organization Jerusalem, ISRAEL 91120	972 2 677 7242	N/A
ISR	RAB01	Rabin Medical Center	Helsinski Committee, Rabin Medical Center	Rabin Medical Center, Jabotinsky Street Petach Tikva, ISRAEL 49100	972 3 937 7218	N/A

Country	Site	Site Full Name	IRB Name	Address	Phone #	FWA #
ISR	RAM01	Rambam Health Care Campus	Helsinski Committee, Rambam Health Care Campus, Haifa, Israel	Rambam Medical Center Rambam Health Care Campus, 8 Ha'Aliya Ha'shniya Street, Bat Galim, Haifa, ISRAEL 3109601	972 4 777 2547	N/A
ISR	SMP01	Sheba Medical Center Pediatrics	The Chaim Sheba Medical Center, Institutional Review Committee (Helsinki Committee)	Chaim Sheba Medical Center Ramat Gan - Tel HaShomer ISRAEL 52621	972 3 530 5997	N/A
ISR	TAP01	Tel Aviv Sourasky Medical Center Pediatrics	The Tel Aviv Sourasky Medical Center Helsinki Committee	Sourasky Medical Center, 6 Weizmann Street, Sourasky Building, Wing E, Floor 2, Tel Aviv ISRAEL 6423906	972 3 697 4924	N/A
ISR	TAS01	Tel Aviv Sourasky Medical Center Adults	The Tel Aviv Sourasky Medical Center Helsinki Committee	Sourasky Medical Center, 6 Weizmann Street, Sourasky Building, Wing E, Floor 2, Tel Aviv ISRAEL 6423906	972 3 697 4924	N/A

BRA: Brazil; ESP: Spain; FRA: France; GBR: Great Britain; ITA: Italy; ISR: Israel; NLD: Netherlands; PRT: Portugal; SGP: Singapore; USA: United States of America

16.1.4 List and Description of Investigators and Sites

The list and description of the investigators and study sites are presented in Appendix 16.1.4.

16.1.5 Signatures of Sponsor's Responsible Medical Officer

The signature the Sponsor's Responsible Medical Officer, is presented in Appendix 16.1.5.

16.1.6 Listing of Patients Receiving Investigational Product(s) from Specific Batches, where more than One Batch was Used

The listing of patients receiving IP from specific batches is presented in Appendix 16.1.6.

16.1.7 Randomization Scheme and Codes

Randomization assignment information is included in Appendix 16.1.7.

16.1.8 Audit Certificates

Audit certificates are presented in Appendix 16.1.8.

16.1.9 Documentation of Statistical Methods (SAP)

The SAP, related addendum, and DMC reports and meeting minutes are presented in Appendix 16.1.9.

16.1.10 Documentation of Inter-laboratory Standardization Methods and Quality Assurance Procedures If Used

Not applicable.

16.1.11 Publications Based on the Study

Publications based on the study are presented in Appendix 16.1.11.

16.1.12 Important Publications Referenced in the Report

Publications referenced in the CSR are included in Appendix 16.1.12.

16.2 Patient Data Listings

Listing Number	Title
16.2.1	Discontinued Patients
16.2.2	Protocol Deviations
16.2.3	Patients Excluded from the Efficacy Analysis
16.2.4	Demographic Data
16.2.5	Compliance and/or Drug Concentration Data
16.2.6	Individual Efficacy Response Data
16.2.7	Adverse Event Listings
16.2.8	Individual Patient Data Listings/Laboratory Measurements

16.2.1 Discontinued Patients

Discontinuation information is presented in Appendix 16.2.1.

16.2.2 Protocol Deviations

Protocol deviations are presented in Appendix 16.2.2.

16.2.3 Patients Excluded from the Efficacy Analysis

No patients were excluded from the efficacy analysis.

16.2.4 Demographic Data

Demographic data is presented in Appendix 16.2.4.

16.2.5 Compliance and/or Drug Concentration Data

Compliance and drug concentration data is presented in Appendix 16.2.5.

16.2.6 Individual Efficacy Response Data

Individual efficacy response data is presented in Appendix 16.2.6.

16.2.7 Adverse Event Listings

Adverse event listings for each patient are presented in Appendix 16.2.7.

16.2.8 Individual Patient Data Listings/Laboratory Measurements

Listings of individual laboratory measurements by patient are presented in Appendix 16.2.8.

16.3 Case Report Forms

Listing Number	Title
16.3.1	CRF's for Deaths, other SAEs, and Withdrawals for AEs
16.3.2	Other CRF's Submitted

16.3.1 CRF's for Deaths, other SAEs, and Withdrawals for AEs

Case Report Forms for deaths, other SAEs, and withdrawals for AEs are presented in Appendix 16.3.1.

16.3.2 Other CRF's Submitted

Not applicable.