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A Study of Clofarabine and Cytarabine for Older Patients With Relapsed or Refractory Acute Myelogenous Leukemia (AML)(CLASSIC I)

This study has been completed.

Sponsor:	Genzyme, a Sanofi Company
Collaborators:	
Information provided by (Responsible Party):	Sanofi (Genzyme, a Sanofi Company)
ClinicalTrials.gov Identifier:	NCT00317642

Purpose

Clofarabine (injection) is approved by the Food and Drug Administration (FDA) for the treatment of pediatric patients 1 to 21 years old with relapsed acute or refractory lymphoblastic leukemia (ALL) who have had at least 2 prior treatment regimens.

There is no recommended standard treatment for relapsed or refractory acute myelogenous leukemia in older patients. Cytarabine is the most commonly used drug to treat these patients. This study will determine if there is benefit by combining clofarabine with cytarabine. Patients will be randomized to receive up to 3 cycles of treatment with either placebo in combination with cytarabine or clofarabine in combination with cytarabine. Randomization was stratified by remission status following the first induction regimen (no remission [i.e., CR1 = refractory] or remission <6 months vs CR1 = remission ≥6 months). CR1 is defined as remission after first pre-study induction regimen. The safety and tolerability of clofarabine in combination with cytarabine and cytarabine alone will be monitored throughout the study.

Condition	Intervention	Phase
Acute Myelogenous Leukemia	Drug: clofarabine (IV formulation) Drug: placebo Drug: cytarabine	Phase 3

Study Type: Interventional

Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Randomized, Safety/Efficacy Study
Official Title: A Phase III Randomized, Double-blind, Controlled Study Comparing Clofarabine and Cytarabine Versus Cytarabine Alone in Adult Patients 55 Years and Older With Acute Myelogenous Leukemia (AML) Who Have Relapsed or Are Refractory After Receiving up to Two Prior Induction Regimens

Further study details as provided by Sanofi (Genzyme, a Sanofi Company):

Primary Outcome Measure:

- Overall Survival - Overall and by Calculated Strata (CSR 7-April-11) [Time Frame: Day 1 (randomization) up to approximately 4 years] [Designated as safety issue: No]
  Overall survival (OS) for the Full Analysis Set (FAS) and for the 2 calculated strata. OS was defined as the number of months from date of randomization until date of death due to any cause.
- Overall Survival - Overall and by Randomized Strata (CSR 9-July-12) [Time Frame: Day 1 (randomization) up to approximately 4 years] [Designated as safety issue: No]
  Overall survival (OS) for the Full Analysis Set (FAS) and for the 2 randomized strata. OS was defined as the number of months from date of randomization until date of death due to any cause.

Secondary Outcome Measures:

- Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11) [Time Frame: Day 12 up to approximately 6 months] [Designated as safety issue: No]
  Percentage of participants whose best response was assessed by the IRRP as complete remission (CR) or complete remission with incomplete peripheral blood count recovery (CRi) using the revised International Working Group for Response Criteria (Cheson 2003). CR is defined on morphologic criteria at a single response assessment: - a bone marrow aspirate or biopsy of <5% blasts, with evidence of normal hematopoiesis; - absence of Auer rods in the blasts that are present; - absence of extramedullary disease; - absence of a unique phenotype determined at the pretreatment specimen, as assessed by immunophenotyping; - only rare evidence of circulating blasts. If present, evidence of a regenerating bone marrow; - recovery of peripheral counts (platelets ≥100*10^9/L and absolute neutrophil count (ANC) ≥1.0*10^9/L). CRi met all criteria for CR except for either residual neutropenia (ANC <1.0*10^9/L) or thrombocytopenia (platelet count <100*10^9/L).
- Duration of Remission (DOR) Per IRRP Assessment-Overall and by Calculated Strata (CSR 7-April-11) [Time Frame: Day 12 to approximately 4 years] [Designated as safety issue: No]
  DOR was defined as the time from first CR or CRi to the date of first objective documentation of disease recurrence, initiation of alternative antileukemic therapy [including hematopoietic stem cell transplant] while in remission, or death due to any cause, whichever occurred first. CR is defined on morphologic criteria at a single response assessment: - a bone marrow aspirate or biopsy of <5% blasts, with evidence of normal hematopoiesis; - absence of Auer rods in the blasts that are present; - absence of extramedullary disease; - absence of a unique phenotype determined at the pretreatment specimen, as assessed by immunophenotyping; - only rare evidence of circulating blasts. If present, evidence of a regenerating bone marrow; - recovery of peripheral counts (platelets ≥100*10^9/L and absolute neutrophil count (ANC) ≥1.0*10^9/L). CRi met all criteria for CR except for either residual neutropenia (ANC <1.0*10^9/L) or thrombocytopenia (platelet count <100*10^9/L).
- Duration of Remission (DOR) Per IRRP Assessment-Overall and by Randomized Strata (CSR 9-July-12) [Time Frame: Day 12 to approximately 4 years] [Designated as safety issue: No]
  DOR was defined as the time from first CR or CRi to the date of first objective documentation of disease recurrence, initiation of alternative antileukemic therapy [including hematopoietic stem cell transplant] while in remission, or death due to any cause, whichever occurred first. CR is defined on morphologic criteria at a single response assessment: - a bone marrow aspirate or biopsy of <5% blasts, with evidence of normal hematopoiesis; - absence of Auer rods in the blasts that are present; - absence of extramedullary disease; - absence of a unique phenotype determined at the pretreatment specimen, as assessed by immunophenotyping; - only rare evidence of circulating blasts. If present, evidence of a regenerating bone marrow; - recovery of peripheral counts (platelets ≥100*10^9/L and absolute neutrophil count (ANC) ≥1.0*10^9/L). CRi met all criteria for CR except for either residual neutropenia (ANC <1.0*10^9/L) or thrombocytopenia (platelet count <100*10^9/L).
- Disease-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11) [Time Frame: Day 12 to approximately 4 years] [Designated as safety issue: No]

Disease-free survival was defined as the time from first complete remission (CR) or complete remission with incomplete peripheral blood count recovery (CRi) until the date of first objective documentation of disease recurrence or death due to any cause, whichever occurred first. See Outcome #3 for definition of CR and CRi. Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.

- Disease-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12) [Time Frame: Day 12 to approximately 4 years] [Designated as safety issue: No]

  Disease-free survival was defined as the time from first complete remission (CR) or complete remission with incomplete peripheral blood count recovery (CRi) until the date of first objective documentation of disease recurrence or death due to any cause, whichever occurred first. See Outcome #3 for definition of CR and CRi. Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
- Event-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11) [Time Frame: Day 1 (randomization) up to approximately 4 years] [Designated as safety issue: No]

  Event-free survival (EFS) was defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
- Event-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12) [Time Frame: Day 1 (randomization) up to approximately 4 years] [Designated as safety issue: No]

  Event-free survival (EFS) was defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
- Four-Month Event-free Survival Per IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11) [Time Frame: Day 1 (randomization) to Day 122] [Designated as safety issue: No]

  Four-month event-free survival (EFS) was defined as achieving an EFS of at least 122 days, where EFS is defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
- Four-Month Event-free Survival Per IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12) [Time Frame: Day 1 (randomization) to Day 122] [Designated as safety issue: No]

  Four-month event-free survival (EFS) was defined as achieving an EFS of at least 122 days, where EFS is defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
- Participants With Adverse Events (CSR 7-April-11) [Time Frame: Day 1 up to a maximum of 4 years (includes up to a maximum of 3 cycles of therapy plus 45 days follow up. Related AEs are followed to resolution.)] [Designated as safety issue: Yes]

  Number of participants with treatment emergent adverse events (TEAEs) or death due to related AE. Related AEs for the combination arm can be related to either clofarabine or cytarabine. Grade 1 = Mild AE, Grade 2 = Moderate AE, Grade 3 = Severe AE, Grade 4 = Life Threatening AE, Grade 5 = Death

Enrollment: 326
Study Start Date: August 2006
Primary Completion Date: January 2012

Study Completion Date: January 2012

Arms	Assigned Interventions
Experimental: clofarabine (IV formulation) and cytarabine Participants received clofarabine (40 mg/m^2) administered as a 1-hour infusion followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour infusion. Participants could receive up to 3 cycles of treatment (induction, re-induction, and consolidation) Complete induction cycle = 5 consecutive days of treatment Re-induction cycle = 5 consecutive days of treatment at the original or modified dose Consolidation cycle = 4 consecutive days of treatment at the original or modified dose	Drug: clofarabine (IV formulation) clofarabine (IV formulation) infusion 40mg/m^2 / day up to 3 cycles Other Names: Clolar® Evoltra® Drug: cytarabine cytarabine IV infusion 1g/m^2/day for up to 3 cycles
Experimental: placebo and cytarabine Participants received placebo administered as a 1-hour infusion followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour infusion. Patients could receive up to 3 cycles of treatment (induction, re-induction, and consolidation)	Drug: placebo placebo (sodium Chloride) 1-hour IV infusion Drug: cytarabine cytarabine IV infusion 1g/m^2/day for up to 3 cycles

Detailed Description:

After screening and eligibility assessment, patients were randomized (in a 1:1 ratio) to receive either clofarabine or matching placebo, in addition to cytarabine. Randomization was stratified by remission status following the first induction regimen (CR1): no remission [i.e., CR1 = refractory] or remission <6 months vs remission ≥6 months. During randomization by interactive voice response system (IVRS), there were 10 participants misclassified to the CR1 <6 months stratum and 12 participants misclassified to CR1 ≥6 months stratum. The error did not affect the participants' treatment, only the stratification. Due to the misclassification, outcomes that used strata in their analysis were analyzed twice: once with the 'randomized stratification' which includes the misclassification and once with the 'calculated stratification' in which participants appear in the 'correct' strata.

Two clinical study reports were written for this study.

1. Clinical study report dated 7 April 2011 includes the entire treatment period of all participants plus much of the follow-up. At that time, 33 participants in the Clofarabine+cytarabine group and 29 participants in the placebo+cytarabine group were still being follow-up post treatment. Results were reported on clinicaltrials.gov in August 2011. Outcomes that used strata reported the 'calculated strata' on clinicaltrials.gov.
2. Clinical study report dated 9 July 2012 includes all patient treatment experience plus all long-term follow-up (a minimum of 2 years from the end of treatment or until the patient died). The study was completed at that time. Outcomes that used strata reported the 'randomized strata' on clinicaltrials.gov. AE records on clinicaltrials.gov reflect the final database.

Outcomes that changed between the two clinical study reports due to the additional long-term follow-up data are reported twice on clinicaltrials.gov (once from each clinical study report) and the appropriate report date is included in the outcome description. Outcomes from the 9 July 2012 report represent more complete data.

Eligibility

Ages Eligible for Study: 55 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Have a diagnosis of Acute Myelogenous Leukemia (AML) according to World Health Organization (WHO) classification
- Relapsed after receiving up to 2 prior induction regimens (i.e. first or second relapse)or are refractory to not more than one prior combination chemotherapy induction regimen
- Be ≥ 55 years of age
- Have an Eastern Cooperative Oncology Group (ECOG) score of 0-2
- Be able to comply with study procedures and follow-up examinations
- Be nonfertile or agree to use birth control during the study through the end of treatment visit and for at least 90 days after the last dose of study drug
- Have adequate liver and renal function as indicated by certain laboratory values

Exclusion Criteria:

- Received previous treatment with clofarabine
- Received bolus, intermediate or high-dose cytarabine as induction therapy unless certain remission criteria are met
- Have received a hematopoietic stem cell transplant (HSCT) within the previous 3 months
- Have moderate or severe graft versus host disease (GVHD), whether acute or chronic
- Are receiving any other chemotherapy or investigational therapy. Patients must have been off prior AML therapy for at least 2-6 weeks prior to entering study.
- Have a psychiatric disorder that would interfere with consent, study participation, or follow-up
- Have an active, uncontrolled infection
- Have any other severe concurrent disease, or have a history of serious organ dysfunction or disease involving the heart, kidney, liver, or other organ system
- Have been diagnosed with another malignancy, unless disease-free for at least 5 years; patients with treated nonmelanoma skin cancer, in situ carcinoma, or cervical intraepithelial neoplasia, regardless of the disease-free duration, are eligible for this study if definitive treatment for the condition has been completed; patients with organ-confined prostate cancer with no evidence of recurrent or progressive disease are eligible if hormonal therapy has been initiated or the malignancy has been surgically removed.
- Have clinical evidence suggestive of central nervous system (CNS) involvement with leukemia unless lumbar puncture confirms absence of leukemic blasts in the cerebrospinal fluid(CSF)

- Known HIV positivity
- Are pregnant or lactating

Contacts and Locations

Locations
- United States, Arizona
  - Mayo Clinical Hospital
    - Scottsdale, Arizona, United States
  - Arizona Cancer Center
    - Tucson, Arizona, United States
- United States, Arkansas
  - University of Arkansas for Medical Sciences, Arkansas Cancer Research Center
    - Little Rock, Arkansas, United States
- United States, California
  - Scripps Cancer Center
    - La Jolla, California, United States
  - University of Southern California, Kenneth Norris Cancer Center
    - Los Angeles, California, United States
  - UCLA School of Medicine
    - Los Angeles, California, United States
  - Stanford Comprehensive Cancer Center
    - Stanford, California, United States
- United States, Colorado
  - University of Colorado Health Science Center
    - Aurora, Colorado, United States
  - Rocky Mountain Cancer Center
    - Denver, Colorado, United States
- United States, Connecticut
  - Cancer Center of Central Connecticut
    - Southington, Connecticut, United States
- United States, Illinois
  - Rush University Medical Center
    - Chicago, Illinois, United States
  - Northwestern University
    - Chicago, Illinois, United States
  - Evanston Northwestern Healthcare
    - Evanston, Illinois, United States
- United States, Kansas
  - University of Kansas Medical Center
    - Kansas City, Kansas, United States
- United States, Kentucky
  - University of Kentucky, Markey Cancer Center
    - Lexington, Kentucky, United States

United States, Louisiana
Louisiana State University Health Science Center
Shreveport, Louisiana, United States
United States, Maine
Harold Alfond Center for Cancer Care
Augusta, Maine, United States
United States, Massachusetts
Beth Israel Deaconess Medical Center
Boston, Massachusetts, United States
United States, Michigan
Josephine Ford Cancer Center
Detroit, Michigan, United States
United States, New Hampshire
Dartmouth Hitchcock Medical Center
Lebanon, New Hampshire, United States
United States, New Jersey
The Cancer Center at Hackensack University Medical Center
Hackensack, New Jersey, United States
United States, New York
Roswell Park Cancer Center
Buffalo, New York, United States
Mt. Sinai School of Medicine
New York, New York, United States
New York Medical Center
Valhalla, New York, United States
United States, North Carolina
Mecklenburg Medical Group
Charlotte, North Carolina, United States
Duke University Medical Center
Durham, North Carolina, United States
Wake Forest University School of Medicine
Winston-Salem, North Carolina, United States
United States, Ohio
Gabrail Cancer Center
Canton, Ohio, United States
United States, Oklahoma
University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma, United States
United States, Oregon
Oregon Health Science University
Portland, Oregon, United States
United States, South Carolina
Medical University of South Carolina
Charleston, South Carolina, United States
United States, Tennessee

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Sarah Cannon Research Institute
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Vanderbilt University Medical Center
Nashville, Tennessee, United States
United States, Texas
UT Southwestern Medical Center, Simmons Comprehensive Cancer Center
Dallas, Texas, United States
MD Anderson Cancer Center
Houston, Texas, United States
Cancer Care Centers of South Texas
San Antonio, Texas, United States
University of Texas Health Sciences Center
San Antonio, Texas, United States
United States, Utah
University of Utah - Huntsman Cancer Institute
Salt Lake City, Utah, United States
United States, West Virginia
West Virginia University Hospitals, Mary Babb Randolph Cancer Center
Morgantown, West Virginia, United States
United States, Wisconsin
Medical College of Wisconsin
Milwaukee, Wisconsin, United States
Canada, New Brunswick
Saint John Regional Hospital
Saint John, New Brunswick, Canada
Canada, Ontario
Juravinski Cancer Center
Hamilton, Ontario, Canada
Canada, Quebec
Hopital Maisonneuve-Rosemont
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Hopital Edouard Herriot
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Azienda Ospedaliera "Antonio Cardarelli"
Napoli, Italy

Investigators

Study Director:	Medical Monitor	Genzyme Corporation

More Information

Results Publications:

Clofarabine + Ara-c improves response rates and event-free survival, not overall survival, in older patients with relapsed/refractory AML compared to Ara-c alone: Updated CLASSIC I study results. H.M. Kantarjian, M. Wetzler, D. Rizzieri, G. J. Schiller, M. H. Jagasia, R. K. Stuart, S. Ganguly, D. Avigan, M. Craig, R. Collins, M. B. Maris, T. Kovacsovics, S. Goldberg, K. Seiter, P. Hari, J. Greiner, N. Vey, C. Recher, F. Ravandi, E.S. Wang, S. Eckert, D. Huebner and S. Faderl. Haematologica - 16th Congress of EHA Abstracts. 2011; 96(S2): 196.

Clofarabine plus cytarabine compared to cytarabine alone in older patients with relapsed or refractory (R/R) acute myelogenous leukemia (AML): Results from the phase III CLASSIC 1 trial. S. Faderl, M. Wetzler, D. Rizzieri, G. J. Schiller, M. H. Jagasia, R. K. Stuart, S. Ganguly, D. Avigan, M. Craig, R. Collins, M. B. Maris, T. Kovacsovics, S. Goldberg, K. Seiter, P. Hari, F. Ravandi, E. S. Wang, S. Eckert, D. Huebner, and H. Kantarjian JCO - ASCO Meeting Abstracts. 2011; 29:6503.

Faderl S, Wetzler M, Rizzieri D, Schiller G, Jagasia M, Stuart R, Ganguly S, Avigan D, Craig M, Collins R, Maris M, Kovacsovics T, Goldberg S, Seiter K, Hari P, Greiner J, Vey N, Recher C, Ravandi F, Wang ES, Vasconcelles M, Huebner D, Kantarjian HM. Clofarabine plus cytarabine compared with cytarabine alone in older patients with relapsed or refractory acute myelogenous leukemia: results from the CLASSIC I Trial. J Clin Oncol. 2012 Jul 10;30(20):2492-9. doi: 10.1200/JCO.2011.37.9743. Epub 2012 May 14.

Ganguly S, Kantarjian HM, Wetzler M, Rizzieri D, Schiller G, Jagasia M, et al. Subsequent hematopoietic stem cell transplantation (HSCT) associated with longer survival in patients with relapsed/refractory (R/R) acute myelogenous leukemia (AML) after Clo+Ara-C or Ara-C alone: a landmark analysis from the CLASSIC I trial. Biol Blood Marrow Transplant 2012;18(2Suppl):S211-S212.

Ganguly S, Kantarjian HM, Wetzler M, Rizzieri D, Schiller G, Jagasia M, et al. Subsequent HSCT in the CLASSIC I Study Associated with Longer Survival in Patients With Relapsed/Refractory AML After Clo+Ara-C Or Ara-C Alone: A Landmark Analysis. Haematologica - 17th Congress of EHA Abstracts. 2012; 97(s1):32

Responsible Party: Genzyme, a Sanofi Company
Study ID Numbers: CLO34100405
2008-001043-19 [EudraCT Number]
Health Authority: United States: Food and Drug Administration
Italy: Ministry of Health
Germany: Federal Institute for Drugs and Medical Devices
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Canada: Health Canada

Study Results

Participant Flow

Pre-Assignment Details	352 patients screened and 326 randomized, 163 to each treatment group. One participant withdrew after being randomized to the Placebo and Cytarabine Group and was excluded from efficacy analysis.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Overall Study

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine
Started	163	163
Full Analysis Set	162 [1]	158 [1]
Received >= 1 Study Drug (Safety Set)	161	155

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine
Completed	41 [2]	28 [2]
Not Completed	122	135
Not Received Either Study Drug	1	3
Physician Decision	15	7
Participant declined treatment	14	3
Adverse Event	17	5
Treatment Failure	56	102
Disease Recurrence	1	2
Death	14	7
Not Continue to Consolidation	2	0
Withdrawal by Subject	0	1
Referred For Transplantation	1	0
AML Not Centrally Confirmed	1	5

[1] AML Centrally Confirmed
[2] achieved remission and completed consolidation

Baseline Characteristics

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Baseline Measures

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Total
Number of Participants	162	158	320
Age, Continuous [units: years] Mean (Standard Deviation)	67.0 (6.36)	67.1 (5.82)	67.0 (6.09)
Gender, Male/Female [units: participants]			
Female	48	57	105
Male	114	101	215
Ethnicity (NIH/OMB) [units: participants]			
Hispanic or Latino	9	6	15
Not Hispanic or Latino	153	152	305
Unknown or Not Reported	0	0	0
Race (NIH/OMB) [units: participants]			
American Indian or Alaska Native	0	0	0
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	7	11	18
White	150	142	292
More than one race	0	0	0
Unknown or Not Reported	2	3	5
Height (cm) [units: centimeter] Mean (Standard Deviation)	171.5 (10.27)	170.5 (8.92)	171.0 (9.62)
Weight(kg) [units: kg] Mean (Standard Deviation)	81.21 (17.862)	83.03 (17.281)	82.11 (17.574)
Body Surface Area (BSA) [units: m^2] Mean (Standard Deviation)	1.941 (0.2383)	1.959 (0.2338)	1.950 (0.2359)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Total
Eastern Cooperative Oncology Group Performance Status [1] [units: Participants]			
ECOG 0	57	48	105
ECOG 1	79	92	171
ECOG 2	26	18	44
Karyotype [2] [units: participants]			
Favorable	1	0	1
Intermediate	65	84	149
Unfavorable	86	70	156
Not Assessed	8	3	11
unknown	2	1	3

[1] Eastern Cooperative Oncology Group Performance Status (ECOG PS) is a scale ranging from 0-5, with 0 (fully active); 1 (capable of light work); 2 (no work but all self-care); 3 (limited self-care); 4 (completely disabled); 5 (dead).

[2] Favorable karyotype was defined as any abnormality of chromosome 16; Intermediate karyotype was defined as normal (no abnormalities); Unfavorable karyotype was defined as any other abnormality

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Overall Survival - Overall and by Calculated Strata (CSR 7-April-11)
Measure Description	Overall survival (OS) for the Full Analysis Set (FAS) and for the 2 calculated strata. OS was defined as the number of months from date of randomization until date of death due to any cause.
Time Frame	Day 1 (randomization) up to approximately 4 years
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS)-all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are calculated according to duration of the first remission based on case report forms (CRF) data and do not include the IVRS mistakes. One participant's strata (placebo group) could not be calculated so the participant was excluded.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine (FAS)	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine (FAS)	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine (FAS)	Placebo and Cytarabine (FAS)	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	157	88	83	74	74

	Clofarabine (IV Formulation) and Cytarabine (FAS)	Placebo and Cytarabine (FAS)	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Overall Survival - Overall and by Calculated Strata (CSR 7-April-11) [units: months] Median (95% Confidence Interval)	6.6 (5.1 to 9.3)	6.4 (4.7 to 7.3)	5.1 (3.5 to 8.7)	5.5 (4.1 to 7.2)	8.7 (5.3 to 11.1)	7.2 (4.6 to 8.9)

Statistical Analysis 1 for Overall Survival - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine (FAS), Placebo and Cytarabine (FAS)
	Comments	Full Analysis Set (FAS) population
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9951
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.00
	Confidence Interval	(2-Sided) 95% 0.78 to 1.28
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Overall Survival - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	Participants stratified by calculated strata remission after first pre-study induction regimen (CR1) < 6 months

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4674
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.13
	Confidence Interval	(2-Sided) 95% 0.81 to 1.57
	Estimation Comments	[Not specified]

Statistical Analysis 3 for Overall Survival - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	Participants stratified by calculated strata CR1>= 6 months
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3963
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.85
	Confidence Interval	(2-Sided) 95% 0.58 to 1.24
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Overall Survival - Overall and by Randomized Strata (CSR 9-July-12)
Measure Description	Overall survival (OS) for the Full Analysis Set (FAS) and for the 2 randomized strata. OS was defined as the number of months from date of randomization until date of death due to any cause.
Time Frame	Day 1 (randomization) up to approximately 4 years
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS) - composed of all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are as randomized by the IVRS, therefore strata include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine (FAS)	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine (FAS)	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.

	Description
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine (FAS)	Placebo and Cytarabine (FAS)	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	158	86	84	76	74
Overall Survival - Overall and by Randomized Strata (CSR 9-July-12) [units: months] Median (95% Confidence Interval)	6.6 (5.1 to 9.3)	6.3 (4.7 to 7.3)	4.8 (2.9 to 7.3)	6.3 (4.1 to 7.8)	9.7 (5.9 to 12.7)	6.6 (4.3 to 8.8)

Statistical Analysis 1 for Overall Survival - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine (FAS), Placebo and Cytarabine (FAS)
	Comments	Full Analysis Set (FAS) population
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8209
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.97
	Confidence Interval	(2-Sided) 95% 0.77 to 1.23

	Estimation Comments	[Not specified]

Statistical Analysis 2 for Overall Survival - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5071
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.11
	Confidence Interval	(2-Sided) 95% 0.81 to 1.53
	Estimation Comments	[Not specified]

Statistical Analysis 3 for Overall Survival - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2906
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.83
	Confidence Interval	(2-Sided) 95% 0.59 to 1.17
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)
Measure Description	Percentage of participants whose best response was assessed by the IRRP as complete remission (CR) or complete remission with incomplete peripheral blood count recovery (CRi) using the revised International Working Group for Response Criteria (Cheson 2003). CR is defined on morphologic criteria at a single response assessment: • a bone marrow aspirate or biopsy of <5% blasts, with evidence of normal hematopoiesis; • absence of Auer rods in the blasts that are present; • absence of extramedullary disease; • absence of a unique phenotype determined at the pretreatment specimen, as assessed by immunophenotyping; • only rare evidence of circulating blasts. If present, evidence of a regenerating bone marrow; • recovery of peripheral counts (platelets ≥100*10^9/L and absolute neutrophil count (ANC) ≥1.0*10^9/L). CRi met all criteria for CR except for either residual neutropenia (ANC <1.0*10^9/L) or thrombocytopenia (platelet count <100*10^9/L).
Time Frame	Day 12 up to approximately 6 months
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS)-all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are calculated according to duration of the first remission based on case report forms (CRF) data and do not include the IVRS mistakes. One participant's strata (placebo group) could not be calculated so the participant was excluded.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.

	Description
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	157	88	83	74	74
Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11) [units: percentage of participants]						
Overall Remission (CR + CRi)	46.9	22.9	45.5	22.9	48.6	23.0
Complete Remission (CR)	35.2	17.8	33.0	18.1	37.8	17.6
CR with incomplete blood count recovery (CRi)	11.7	5.1	12.5	4.8	10.8	5.4

Statistical Analysis 1 for Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine, Placebo and Cytarabine
	Comments	Full Analysis Set (FAS) population - overall remission (OR)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 2 for Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine, Placebo and Cytarabine
	Comments	Full Analysis Set (FAS) population - Complete Remission (CR)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0005
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 3 for Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	Participants stratified by calculated strata - CR1 <6 months [Overall Remission (CR+CRi)]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0022
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

Statistical Analysis 4 for Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	Participants stratified by calculated strata - CR1 >=6 months [Overall Remission (CR+CRi)]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0019
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

Statistical Analysis 5 for Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	Participants stratified by calculated strata - CR1 <6 months [Complete Remission (CR)]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0353
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

Statistical Analysis 6 for Best Response Per Independent Response Review Panel (IRRP) Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	Participants stratified by calculated strata - CR1 >=6 months [Complete Remission (CR)]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0096
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Duration of Remission (DOR) Per IRRP Assessment-Overall and by Calculated Strata (CSR 7-April-11)
Measure Description	DOR was defined as the time from first CR or CRi to the date of first objective documentation of disease recurrence, initiation of alternative antileukemic therapy [including hematopoietic stem cell transplant] while in remission, or death due to any cause, whichever occurred first. CR is defined on morphologic criteria at a single response assessment: • a bone marrow aspirate or biopsy of <5% blasts, with evidence of normal hematopoiesis; • absence of Auer rods in the blasts that are present; • absence of extramedullary disease; • absence of a unique phenotype determined at the pretreatment specimen, as assessed by immunophenotyping; • only rare evidence of circulating blasts. If present, evidence of a regenerating bone marrow; • recovery of peripheral counts (platelets ≥100*10^9/L and absolute neutrophil count (ANC) ≥1.0*10^9/L). CRi met all criteria for CR except for either residual neutropenia (ANC <1.0*10^9/L) or thrombocytopenia (platelet count <100*10^9/L).
Time Frame	Day 12 to approximately 4 years
Safety Issue?	No

Analysis Population Description

Participants in the FAS who achieved OR (CR + CRi). Strata are calculated according to duration of the first remission based on case report forms (CRF) data and do not include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	76	36	40	19	36	17
Duration of Remission (DOR) Per IRRP Assessment-Overall and by Calculated Strata (CSR 7-April-11) [units: months]	7.6 (5.4 to 11.5)	3.8 (3.3 to 12.1)	5.7 (5.3 to 7.7)	6.3 (2.3 to 7.2)	11.5 (6.8 to 15.5)	3.8 (3.3 to NA) [1]

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Median (95% Confidence Interval)						

[1] N/A = There were an insufficient number of events to allow estimation of the upper limit.

5. Secondary Outcome Measure:

Measure Title	Duration of Remission (DOR) Per IRRP Assessment-Overall and by Randomized Strata (CSR 9-July-12)
Measure Description	DOR was defined as the time from first CR or CRi to the date of first objective documentation of disease recurrence, initiation of alternative antileukemic therapy [including hematopoietic stem cell transplant] while in remission, or death due to any cause, whichever occurred first. CR is defined on morphologic criteria at a single response assessment: • a bone marrow aspirate or biopsy of <5% blasts, with evidence of normal hematopoiesis; • absence of Auer rods in the blasts that are present; • absence of extramedullary disease; • absence of a unique phenotype determined at the pretreatment specimen, as assessed by immunophenotyping; • only rare evidence of circulating blasts. If present, evidence of a regenerating bone marrow; • recovery of peripheral counts (platelets ≥100*10^9/L and absolute neutrophil count (ANC) ≥1.0*10^9/L). CRi met all criteria for CR except for either residual neutropenia (ANC <1.0*10^9/L) or thrombocytopenia (platelet count <100*10^9/L).
Time Frame	Day 12 to approximately 4 years
Safety Issue?	No

Analysis Population Description

Participants in the FAS who achieved OR (CR + CRi). Strata are as randomized by the IVRS, therefore strata include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.

	Description
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	76	36	36	20	40	16
Duration of Remission (DOR) Per IRRP Assessment-Overall and by Randomized Strata (CSR 9-July-12) [units: months] Median (95% Confidence Interval)	7.7 (5.7 to 11.5)	3.8 (3.3 to 12.1)	6.7 (4.0 to 8.8)	6.3 (2.3 to 7.2)	10.2 (6.8 to 20.2)	3.8 (3.3 to NA) [1]

[1] There were an insufficient number of events to allow estimation of the upper limit.

6. Secondary Outcome Measure:

Measure Title	Disease-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)
Measure Description	Disease-free survival was defined as the time from first complete remission (CR) or complete remission with incomplete peripheral blood count recovery (CRi) until the date of first objective documentation of disease recurrence or death due to any cause, whichever occurred first. See Outcome #3 for definition of CR and CRi. Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
Time Frame	Day 12 to approximately 4 years
Safety Issue?	No

Analysis Population Description

Participants in the FAS who achieved OR (CR + CRi). Strata are calculated according to duration of the first remission based on case report forms (CRF) data and do not include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

	Description
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	76	36	40	19	36	17
Disease-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11) [units: months] Median (95% Confidence Interval)	8.1 (6.7 to 10.3)	7.0 (3.9 to 12.1)	5.7 (4.4 to 9.7)	6.7 (3.9 to 8.1)	10.3 (7.5 to 15.5)	9.1 (3.7 to NA) [1]

[1] NA = There were an insufficient number of events to allow estimation of the upper limit.

7. Secondary Outcome Measure:

Measure Title	Disease-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)
Measure Description	Disease-free survival was defined as the time from first complete remission (CR) or complete remission with incomplete peripheral blood count recovery (CRi) until the date of first objective documentation of disease recurrence or death due to any cause, whichever occurred first. See Outcome #3 for definition of CR and CRi. Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
Time Frame	Day 12 to approximately 4 years
Safety Issue?	No

Analysis Population Description

Participants in the FAS who achieved OR (CR + CRi). Strata are as randomized by the IVRS, therefore strata include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	76	36	36	20	40	16

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Disease-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12) [units: months] Median (95% Confidence Interval)	9.5 (6.9 to 15.4)	7.0 (3.9 to 9.8)	6.7 (3.9 to 9.7)	6.7 (3.9 to 8.1)	15.4 (9.2 to 20.5)	9.2 (3.7 to 13.1)

8. Secondary Outcome Measure:

Measure Title	Event-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)
Measure Description	Event-free survival (EFS) was defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
Time Frame	Day 1 (randomization) up to approximately 4 years
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS)-all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are calculated according to duration of the first remission based on case report forms (CRF) data and do not include the IVRS mistakes. One participant's strata (placebo group) could not be calculated so the participant was excluded.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.

	Description
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	157	88	83	74	74
Event-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11) [units: months] Median (95% Confidence Interval)	1.9 (1.1 to 2.9)	1.0 (0.9 to 1.1)	1.4 (1.0 to 2.9)	1.0 (0.7 to 1.2)	2.0 (1.2 to 6.6)	1.0 (0.9 to 1.2)

Statistical Analysis 1 for Event-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine, Placebo and Cytarabine
	Comments	Full Analysis Set (FAS) population.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.63
	Confidence Interval	(2-Sided) 95% 0.49 to 0.80
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Event-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	Participants stratified by randomization strata CR1 <6 months
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0131
	Comments	[Not specified]
	Method	Log Rank
	Comments	Comparison P-value is from a log-rank test with no strata
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.67
	Confidence Interval	(2-Sided) 95%

		0.49 to 0.93
	Estimation Comments	[Not specified]

Statistical Analysis 3 for Event-free Survival by IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	Participants stratified by randomization strata CR1 >=6 months
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0022
	Comments	[Not specified]
	Method	Log Rank
	Comments	Comparison p-value is from a log-rank test with no strata.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.57
	Confidence Interval	(2-Sided) 95% 0.40 to 0.83
	Estimation Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Event-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)
Measure Description	Event-free survival (EFS) was defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
Time Frame	Day 1 (randomization) up to approximately 4 years
Safety Issue?	No

Analysis Population Description

Full Analysis Set - composed of all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are as randomized by the IVRS, therefore strata include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	158	86	84	76	74
Event-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12) [units: months] Median (95% Confidence Interval)	1.9 (1.1 to 2.9)	1.0 (0.8 to 1.1)	1.1 (0.8 to 2.5)	1.0 (0.7 to 1.2)	2.8 (1.2 to 8.1)	1.0 (0.8 to 1.2)

Statistical Analysis 1 for Event-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine, Placebo and Cytarabine
	Comments	Full Analysis Set (FAS) population.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<.0001
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.63
	Confidence Interval	(2-Sided) 95% 0.49 to 0.79
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Event-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0486
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.73
	Confidence Interval	(2-Sided) 95% 0.53 to 1.01
	Estimation Comments	[Not specified]

Statistical Analysis 3 for Event-free Survival by IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.52
	Confidence Interval	(2-Sided) 95% 0.37 to 0.74
	Estimation Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Four-Month Event-free Survival Per IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)
Measure Description	Four-month event-free survival (EFS) was defined as achieving an EFS of at least 122 days, where EFS is defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
Time Frame	Day 1 (randomization) to Day 122
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS)-all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are calculated according to duration of the first remission based on case report forms (CRF) data and do not include the IVRS mistakes. One participant's strata (placebo group) could not be calculated so the participant was excluded.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

	Description
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	157	88	83	74	74
Four-Month Event-free Survival Per IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11) [units: percentage of participants]	37.7	16.6	35.2	16.9	40.5	16.2

Statistical Analysis 1 for Four-Month Event-free Survival Per IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine, Placebo and Cytarabine
	Comments	Full Analysis Set (FAS) population
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 2 for Four-Month Event-free Survival Per IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	Participants stratified by randomization strata CR1 <6 months.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0088
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

Statistical Analysis 3 for Four-Month Event-free Survival Per IRRP Assessment - Overall and by Calculated Strata (CSR 7-April-11)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	Participants stratified by randomization strata CR1 >=6 months
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0017
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Four-Month Event-free Survival Per IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Measure Description	Four-month event-free survival (EFS) was defined as achieving an EFS of at least 122 days, where EFS is defined as the time from randomization to the date of treatment failure, first disease recurrence (for participants who achieved remission), or death due to any cause, whichever occurred first. Treatment Failure - ≥5% leukemic blasts by bone marrow exam, with no evidence of hematologic response (ie, <30% decrease in % leukemic blasts). Disease recurrence - reappearance of leukemic blasts in the peripheral blood, confirmed by ≥5% blasts in the bone marrow, and reappearance or development of pathologically proven extramedullary disease.
Time Frame	Day 1 (randomization) to Day 122
Safety Issue?	No

Analysis Population Description

Full Analysis Set - composed of all randomized participants whose baseline AML diagnosis was centrally confirmed. Strata are as randomized by the IVRS, that is the strata include the IVRS mistakes.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine - In Stratum < 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine - In Stratum < 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Clofarabine and Cytarabine In Stratum >= 6 Months	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.

	Description
Placebo and Cytarabine In Stratum >= 6 Months	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Clofarabine and Cytarabine - In Stratum < 6 Months	Placebo and Cytarabine - In Stratum < 6 Months	Clofarabine and Cytarabine In Stratum >= 6 Months	Placebo and Cytarabine In Stratum >= 6 Months
Number of Participants Analyzed	162	158	86	84	76	74
Four-Month Event-free Survival Per IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12) [units: percentage of participants]	38.9	17.1	31.4	17.9	47.4	16.2

Statistical Analysis 1 for Four-Month Event-free Survival Per IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine (IV Formulation) and Cytarabine, Placebo and Cytarabine
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Statistical Analysis 2 for Four-Month Event-free Survival Per IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine - In Stratum < 6 Months, Placebo and Cytarabine - In Stratum < 6 Months
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0506
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

Statistical Analysis 3 for Four-Month Event-free Survival Per IRRP Assessment - Overall and by Randomized Strata (CSR 9-July-12)

Statistical Analysis Overview	Comparison Groups	Clofarabine and Cytarabine In Stratum >= 6 Months, Placebo and Cytarabine In Stratum >= 6 Months
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

12. Secondary Outcome Measure:

Measure Title	Participants With Adverse Events (CSR 7-April-11)
Measure Description	Number of participants with treatment emergent adverse events (TEAEs) or death due to related AE. Related AEs for the combination arm can be related to either clofarabine or cytarabine. Grade 1 = Mild AE, Grade 2 = Moderate AE, Grade 3 = Severe AE, Grade 4 = Life Threatening AE, Grade 5 = Death
Time Frame	Day 1 up to a maximum of 4 years (includes up to a maximum of 3 cycles of therapy plus 45 days follow up. Related AEs are followed to resolution.)
Safety Issue?	Yes

Analysis Population Description

Safety Set - Participants in the Full Analysis Set (FAS) who received at least 1 dose of study drug.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.

Measured Values

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine
Number of Participants Analyzed	161	155
Participants With Adverse Events (CSR 7-April-11) [units: participants]		
Any Treatment Emergent AE	161	155
Any Related Treatment Emergent AE	157	133
Any Treatment Emergent Grade >=3 AE	157	133
Any Related Treatment Related Grade >=3 AE	127	83
Discontinue of study medication due to AE	17	5
Discontinue of study medication due to related AE	14	3

Reported Adverse Events

Time Frame	Day 1 up to a maximum of 4 years (includes up to a maximum of 3 cycles of therapy plus 45 days follow up. Related AEs are followed to resolution.)
Additional Description	In the event a single participant has experienced both a serious and a non-serious form of the same adverse event term, the individual has been included in the numerator ("number of affected participants") of both adverse event tables. Adverse event information is from the final database supporting the clinical study report dated 9-July-12.

Reporting Groups

	Description
Clofarabine (IV Formulation) and Cytarabine	Participants received clofarabine 40 mg/m^2 administered as a 1-hour intravenous (IV) infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction (if the participant had not achieved remission following induction but hematological improvement was noted), and consolidation.
Placebo and Cytarabine	Participants received placebo (sodium chloride) administered as a 1-hour IV infusion, followed 3 hours later (from end of infusion) by cytarabine 1 g/m^2 administered as a 2-hour IV infusion for 5 days (induction and re-induction) or 4 days (consolidation). Participants could receive up to 3 cycles of treatment: induction, re-induction, and consolidation.
Overall	Combined total for the two Arms/Groups

Serious Adverse Events

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	97/161 (60.25%)	76/155 (49.03%)	173/316 (54.75%)
Blood and lymphatic system disorders			
Bone marrow failure [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Febrile neutropenia [A] †	25/161 (15.53%)	19/155 (12.26%)	44/316 (13.92%)
Leukopenia [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Lymphadenitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Neutropenia [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Pancytopenia [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Thrombocytopenia [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Cardiac disorders			
Acute myocardial infarction [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Angina pectoris [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Atrial fibrillation [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Atrial flutter [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bradycardia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cardiac arrest [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Cardiac failure [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cardiac failure congestive [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Cardio-respiratory arrest [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Cardiogenic shock [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Myocardial infarction [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Myocardial ischaemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pericarditis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Stress cardiomyopathy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Supraventricular tachycardia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Tachycardia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Eye disorders			
Blindness unilateral [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gastrointestinal disorders			
Abdominal pain [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Caecitis [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Colitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Diarrhoea [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Gastrointestinal haemorrhage [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Lower gastrointestinal haemorrhage [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Melaena [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
General disorders			
Asthenia [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Death [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Fatigue [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Generalised oedema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hypothermia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Inflammation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Multi-organ failure [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Oedema peripheral [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pain [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pyrexia [A] †	7/161 (4.35%)	9/155 (5.81%)	16/316 (5.06%)
Hepatobiliary disorders			
Venoocclusive liver disease [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Immune system disorders			
Anaphylactic reaction [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Graft versus host disease [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Infections and infestations			
Alpha haemolytic streptococcal infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Appendicitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bacteraemia [A] †	7/161 (4.35%)	3/155 (1.94%)	10/316 (3.16%)
Bacterial infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bacterial sepsis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Bronchopulmonary aspergillosis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Cellulitis [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)
Clostridial infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Clostridium difficile colitis [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Corynebacterium sepsis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Device related infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Diverticulitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Enterobacter bacteraemia [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Enterobacter sepsis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Enterococcal bacteraemia [A] †	6/161 (3.73%)	1/155 (0.65%)	7/316 (2.22%)
Enterococcal sepsis [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Escherichia bacteraemia [A] †	4/161 (2.48%)	0/155 (0%)	4/316 (1.27%)
Escherichia infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Escherichia sepsis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Fungal infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Haematoma infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Herpes zoster [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Keratitis herpetic [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Klebsiella bacteraemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Klebsiella sepsis [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lobar pneumonia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Neutropenic sepsis [A] †	4/161 (2.48%)	0/155 (0%)	4/316 (1.27%)
Oral herpes [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Parainfluenzae virus infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pneumonia [A] †	13/161 (8.07%)	12/155 (7.74%)	25/316 (7.91%)
Pneumonia bacterial [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Pneumonia fungal [A] †	5/161 (3.11%)	0/155 (0%)	5/316 (1.58%)
Pneumonia viral [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pseudomonal bacteraemia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Sepsis [A] †	8/161 (4.97%)	3/155 (1.94%)	11/316 (3.48%)
Sepsis syndrome [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Septic shock [A] †	6/161 (3.73%)	0/155 (0%)	6/316 (1.9%)
Serratia sepsis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Sinusitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Staphylococcal bacteraemia [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Staphylococcal infection [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Staphylococcal scalded skin syndrome [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Staphylococcal sepsis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Streptococcal bacteraemia [A] †	4/161 (2.48%)	0/155 (0%)	4/316 (1.27%)
Streptococcal sepsis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Systemic candida [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Upper respiratory fungal infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Urinary tract infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Urinary tract infection bacterial [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Urinary tract infection enterococcal [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Zygomycosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Injury, poisoning and procedural complications			
Femoral neck fracture [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Refractoriness to platelet transfusion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Subdural haematoma [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Investigations			
Aspartate aminotransferase increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood bilirubin increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood phosphorus decreased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ejection fraction decreased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Electrocardiogram QT prolonged [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Lipase increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Troponin I increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
White blood cell count decreased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Metabolism and nutrition disorders			
Acidosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dehydration [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Fluid overload [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hyperuricaemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hypokalaemia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Metabolic acidosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Tumour lysis syndrome [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Musculoskeletal and connective tissue disorders			
Back pain [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Muscle disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Osteoarthritis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia [A] †	4/161 (2.48%)	5/155 (3.23%)	9/316 (2.85%)
Leukaemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neoplasm malignant [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Nervous system disorders			
Cerebral haemorrhage [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Cerebral infarction [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Cerebrovascular accident [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Convulsion [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Encephalopathy [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Hypoxic-ischaemic encephalopathy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neuropathy peripheral [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neurotoxicity [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Peripheral sensorimotor neuropathy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Somnolence [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Status epilepticus [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Syncope [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Psychiatric disorders			
Agitation [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Confusional state [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Mental status changes [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Renal and urinary disorders			
Anuria [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Haematuria [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Renal failure [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Renal failure acute [A] †	5/161 (3.11%)	1/155 (0.65%)	6/316 (1.9%)
Renal failure chronic [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Renal infarct [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome [A] †	4/161 (2.48%)	0/155 (0%)	4/316 (1.27%)
Acute respiratory failure [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Dyspnoea [A] †	1/161 (0.62%)	3/155 (1.94%)	4/316 (1.27%)
Epistaxis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Haemoptysis [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Hypoxia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Interstitial lung disease [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lung infiltration [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Pneumonia aspiration [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pulmonary alveolar haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pulmonary haemorrhage [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Pulmonary oedema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Respiratory distress [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Respiratory failure [A] †	1/161 (0.62%)	4/155 (2.58%)	5/316 (1.58%)
Skin and subcutaneous tissue disorders			
Drug eruption [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Exfoliative rash [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Generalised erythema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Palmar-plantar erythrodysaesthesia syndrome [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Rash [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Toxic epidermal necrolysis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vascular disorders			
Deep vein thrombosis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Hypertension [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Hypotension [A] †	4/161 (2.48%)	4/155 (2.58%)	8/316 (2.53%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 14.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	161/161 (100%)	154/155 (99.35%)	315/316 (99.68%)
Blood and lymphatic system disorders			
Anaemia [A] †	26/161 (16.15%)	18/155 (11.61%)	44/316 (13.92%)
Coagulopathy [A] †	10/161 (6.21%)	1/155 (0.65%)	11/316 (3.48%)
Disseminated intravascular coagulation [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Febrile bone marrow aplasia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Febrile neutropenia [A] †	58/161 (36.02%)	35/155 (22.58%)	93/316 (29.43%)
Haemoglobinaemia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Hypercoagulation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Hyperfibrinogenaemia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Hypofibrinogenaemia [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Hypoprothrombinaemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Leukocytosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Leukopenia [A] †	9/161 (5.59%)	7/155 (4.52%)	16/316 (5.06%)
Lymph node pain [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Lymphadenopathy [A] †	3/161 (1.86%)	5/155 (3.23%)	8/316 (2.53%)
Lymphatic disorder [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Monocytosis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Neutropenia [A] †	17/161 (10.56%)	10/155 (6.45%)	27/316 (8.54%)
Pancytopenia [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Splenomegaly [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Thrombocytopenia [A] †	27/161 (16.77%)	23/155 (14.84%)	50/316 (15.82%)
Cardiac disorders			
Angina pectoris [A] †	5/161 (3.11%)	2/155 (1.29%)	7/316 (2.22%)
Aortic valve calcification [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Aortic valve incompetence [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Aortic valve stenosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Arrhythmia [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Arrhythmia supraventricular [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Atrial fibrillation [A] †	6/161 (3.73%)	3/155 (1.94%)	9/316 (2.85%)
Atrial flutter [A] †	5/161 (3.11%)	0/155 (0%)	5/316 (1.58%)
Atrioventricular block [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Atrioventricular block first degree [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Bradycardia [A] †	3/161 (1.86%)	14/155 (9.03%)	17/316 (5.38%)
Bundle branch block left [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Bundle branch block right [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Cardiac aneurysm [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cardiac failure [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cardiac failure congestive [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Cardiac valve disease [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Cardiomegaly [A] †	4/161 (2.48%)	0/155 (0%)	4/316 (1.27%)
Conduction disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Diastolic dysfunction [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Dilatation atrial [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dilatation ventricular [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Extrasystoles [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Heart valve incompetence [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Intracardiac thrombus [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ischaemic cardiomyopathy [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Left atrial dilatation [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Left ventricular dysfunction [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Left ventricular hypertrophy [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Mitral valve incompetence [A] †	4/161 (2.48%)	3/155 (1.94%)	7/316 (2.22%)
Myocardial infarction [A] †	1/161 (0.62%)	4/155 (2.58%)	5/316 (1.58%)
Myocardial ischaemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nodal arrhythmia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Palpitations [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Pericardial effusion [A] †	3/161 (1.86%)	6/155 (3.87%)	9/316 (2.85%)
Pulmonary valve incompetence [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Sinus arrhythmia [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Sinus bradycardia [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Sinus tachycardia [A] †	12/161 (7.45%)	6/155 (3.87%)	18/316 (5.7%)
Supraventricular extrasystoles [A] †	1/161 (0.62%)	3/155 (1.94%)	4/316 (1.27%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Supraventricular tachycardia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Tachycardia [A] †	25/161 (15.53%)	14/155 (9.03%)	39/316 (12.34%)
Tricuspid valve incompetence [A] †	3/161 (1.86%)	3/155 (1.94%)	6/316 (1.9%)
Ventricular arrhythmia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ventricular extrasystoles [A] †	4/161 (2.48%)	2/155 (1.29%)	6/316 (1.9%)
Ventricular hypertrophy [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ventricular hypokinesia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ventricular tachycardia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Congenital, familial and genetic disorders			
Atrial septal defect [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hydrocele [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ear and labyrinth disorders			
Cerumen impaction [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ear congestion [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ear pain [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Hypoacusis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Tinnitus [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Vertigo [A] †	4/161 (2.48%)	2/155 (1.29%)	6/316 (1.9%)
Endocrine disorders			
Adrenal disorder [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Adrenal insufficiency [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cushingoid [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hyperadrenalism [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Hypothyroidism [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Thyroid mass [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Eye disorders			
Blepharitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Cataract [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Conjunctival cyst [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Conjunctival haemorrhage [A] †	5/161 (3.11%)	3/155 (1.94%)	8/316 (2.53%)
Conjunctival hyperaemia [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Conjunctival pallor [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Conjunctivitis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Diplopia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Dry eye [A] †	7/161 (4.35%)	7/155 (4.52%)	14/316 (4.43%)
Erythema of eyelid [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Eye haemorrhage [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Eye irritation [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Eye pain [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Eye swelling [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Eyelid oedema [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Eyelid ptosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gaze palsy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lacrimation increased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Miosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ocular dysmetria [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ocular hyperaemia [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Ocular icterus [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Optic neuropathy [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Papilloedema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Periorbital oedema [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Photophobia [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Pupillary reflex impaired [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Pupils unequal [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Retinal haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Scleral disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Scleral haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Scleral oedema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vision blurred [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Visual acuity reduced [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Visual impairment [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Vitreous detachment [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Vitreous floaters [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Gastrointestinal disorders			

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Abdominal discomfort [A] †	5/161 (3.11%)	3/155 (1.94%)	8/316 (2.53%)
Abdominal distension [A] †	18/161 (11.18%)	13/155 (8.39%)	31/316 (9.81%)
Abdominal hernia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Abdominal pain [A] †	30/161 (18.63%)	18/155 (11.61%)	48/316 (15.19%)
Abdominal pain lower [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Abdominal pain upper [A] †	5/161 (3.11%)	6/155 (3.87%)	11/316 (3.48%)
Abdominal tenderness [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Anal inflammation [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Aphthous stomatitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ascites [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Caecitis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Chapped lips [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cheilitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Colitis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Colonic polyp [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Colonic pseudo-obstruction [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Constipation [A] †	66/161 (40.99%)	72/155 (46.45%)	138/316 (43.67%)
Crohn's disease [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Diarrhoea [A] †	109/161 (67.7%)	63/155 (40.65%)	172/316 (54.43%)
Diverticulum [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dry mouth [A] †	9/161 (5.59%)	6/155 (3.87%)	15/316 (4.75%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Dyspepsia [A] †	12/161 (7.45%)	19/155 (12.26%)	31/316 (9.81%)
Dysphagia [A] †	7/161 (4.35%)	4/155 (2.58%)	11/316 (3.48%)
Epigastric discomfort [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Eructation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Faecal incontinence [A] †	5/161 (3.11%)	5/155 (3.23%)	10/316 (3.16%)
Faeces discoloured [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Flatulence [A] †	10/161 (6.21%)	4/155 (2.58%)	14/316 (4.43%)
Gastric antral vascular ectasia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Gastritis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gastrointestinal haemorrhage [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Gastrointestinal inflammation [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gastrointestinal sounds abnormal [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Gastrooesophageal reflux disease [A] †	2/161 (1.24%)	5/155 (3.23%)	7/316 (2.22%)
Gingival bleeding [A] †	5/161 (3.11%)	2/155 (1.29%)	7/316 (2.22%)
Gingival cyst [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Gingival pain [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Gingivitis [A] †	6/161 (3.73%)	1/155 (0.65%)	7/316 (2.22%)
Glossodynia [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)
Haematemesis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Haematochezia [A] †	5/161 (3.11%)	3/155 (1.94%)	8/316 (2.53%)
Haemorrhoidal haemorrhage [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Haemorrhoids [A] †	13/161 (8.07%)	9/155 (5.81%)	22/316 (6.96%)
Hiatus hernia [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Hypoaesthesia oral [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Ileus [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Inguinal hernia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Intestinal dilatation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Intestinal obstruction [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Lip blister [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Lip dry [A] †	4/161 (2.48%)	5/155 (3.23%)	9/316 (2.85%)
Lip haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Lip ulceration [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Melaena [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Mouth haemorrhage [A] †	11/161 (6.83%)	7/155 (4.52%)	18/316 (5.7%)
Mouth ulceration [A] †	3/161 (1.86%)	9/155 (5.81%)	12/316 (3.8%)
Mucous stools [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Nausea [A] †	117/161 (72.67%)	82/155 (52.9%)	199/316 (62.97%)
Neutropenic colitis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Odynophagia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Oesophageal dilatation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Oesophageal pain [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Oesophagitis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Oral disorder [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Oral mucosal discolouration [A] †	1/161 (0.62%)	3/155 (1.94%)	4/316 (1.27%)
Oral mucosal erythema [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Oral pain [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Pancreatic mass [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pancreatitis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Parotid gland enlargement [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Poor dental condition [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Proctalgia [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Rectal haemorrhage [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Rectal ulcer [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Retching [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Salivary hypersecretion [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Stomatitis [A] †	17/161 (10.56%)	10/155 (6.45%)	27/316 (8.54%)
Tongue blistering [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tongue coated [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tongue discolouration [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Tongue exfoliation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tongue haematoma [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Tongue ulceration [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tooth disorder [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Toothache [A] †	8/161 (4.97%)	3/155 (1.94%)	11/316 (3.48%)
Umbilical hernia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Upper gastrointestinal haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vomiting [A] †	71/161 (44.1%)	42/155 (27.1%)	113/316 (35.76%)
General disorders			
Adverse event [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Asthenia [A] †	32/161 (19.88%)	33/155 (21.29%)	65/316 (20.57%)
Catheter site discharge [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Catheter site erosion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Catheter site erythema [A] †	6/161 (3.73%)	13/155 (8.39%)	19/316 (6.01%)
Catheter site haematoma [A] †	4/161 (2.48%)	0/155 (0%)	4/316 (1.27%)
Catheter site haemorrhage [A] †	6/161 (3.73%)	4/155 (2.58%)	10/316 (3.16%)
Catheter site inflammation [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Catheter site oedema [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Catheter site pain [A] †	12/161 (7.45%)	9/155 (5.81%)	21/316 (6.65%)
Catheter site pruritus [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Catheter site rash [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Catheter site related reaction [A] †	2/161 (1.24%)	5/155 (3.23%)	7/316 (2.22%)
Catheter site swelling [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Chest discomfort [A] †	4/161 (2.48%)	4/155 (2.58%)	8/316 (2.53%)
Chest pain [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Chills [A] †	38/161 (23.6%)	23/155 (14.84%)	61/316 (19.3%)
Crepitations [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cyst [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Device occlusion [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Discomfort [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Early satiety [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Face oedema [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Facial pain [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Fatigue [A] †	57/161 (35.4%)	49/155 (31.61%)	106/316 (33.54%)
Feeling cold [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Feeling hot [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Gait disturbance [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
General physical health deterioration [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Generalised oedema [A] †	9/161 (5.59%)	4/155 (2.58%)	13/316 (4.11%)
Hypothermia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Infusion site discolouration [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Infusion site induration [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Injection site haemorrhage [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Injection site inflammation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Injection site pain [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Injection site reaction [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Malaise [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Mass [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Medical device complication [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Mucosal dryness [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Mucosal inflammation [A] †	21/161 (13.04%)	19/155 (12.26%)	40/316 (12.66%)
Nodule [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Non-cardiac chest pain [A] †	6/161 (3.73%)	3/155 (1.94%)	9/316 (2.85%)
Oedema [A] †	4/161 (2.48%)	5/155 (3.23%)	9/316 (2.85%)
Oedema peripheral [A] †	82/161 (50.93%)	71/155 (45.81%)	153/316 (48.42%)
Pain [A] †	22/161 (13.66%)	8/155 (5.16%)	30/316 (9.49%)
Pyrexia [A] †	53/161 (32.92%)	39/155 (25.16%)	92/316 (29.11%)
Tenderness [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Thrombosis in device [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Visceral oedema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hepatobiliary disorders			
Bile duct stone [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cholecystitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cholelithiasis [A] †	4/161 (2.48%)	4/155 (2.58%)	8/316 (2.53%)
Dilatation intrahepatic duct acquired [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gallbladder polyp [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hepatic cyst [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hepatic failure [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hepatic function abnormal [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hepatic lesion [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Hepatic steatosis [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Hepatitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hepatomegaly [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)
Hepatosplenomegaly [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Hepatotoxicity [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hyperbilirubinaemia [A] †	15/161 (9.32%)	12/155 (7.74%)	27/316 (8.54%)
Jaundice [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Immune system disorders			
Anaphylactic reaction [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Drug hypersensitivity [A] †	9/161 (5.59%)	1/155 (0.65%)	10/316 (3.16%)
Hypogammaglobulinaemia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Infections and infestations			
Abscess limb [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Acute sinusitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Alpha haemolytic streptococcal infection [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Anal abscess [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Anorectal infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bacteraemia [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Bacterial infection [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bacterial sepsis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Bacteriuria [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bronchopulmonary aspergillosis [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Bullous impetigo [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Candida pneumonia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Candidiasis [A] †	6/161 (3.73%)	3/155 (1.94%)	9/316 (2.85%)
Catheter site cellulitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Catheter site infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cellulitis [A] †	5/161 (3.11%)	9/155 (5.81%)	14/316 (4.43%)
Clostridial infection [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Clostridium difficile colitis [A] †	5/161 (3.11%)	3/155 (1.94%)	8/316 (2.53%)
Cystitis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Cystitis bacterial [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Cytomegalovirus infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cytomegalovirus viraemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Device related infection [A] †	6/161 (3.73%)	5/155 (3.23%)	11/316 (3.48%)
Diarrhoea infectious [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Diverticulitis [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Enterobacter bacteraemia [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Enterococcal bacteraemia [A] †	9/161 (5.59%)	3/155 (1.94%)	12/316 (3.8%)
Enterococcal infection [A] †	4/161 (2.48%)	2/155 (1.29%)	6/316 (1.9%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Enterococcal sepsis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Escherichia bacteraemia [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Escherichia infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Escherichia sepsis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Escherichia urinary tract infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Eye infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Eye infection fungal [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Eye infection staphylococcal [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Folliculitis [A] †	1/161 (0.62%)	6/155 (3.87%)	7/316 (2.22%)
Fungal infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Fungal skin infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Furuncle [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Gastroenteritis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Genital herpes [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hepatosplenic candidiasis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Herpes simplex [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Herpes zoster [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Klebsiella bacteraemia [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Lobar pneumonia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Localised infection [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lung infection [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Lung infection pseudomonal [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Micrococcus infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nasopharyngitis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Oesophageal candidiasis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Onychomycosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Oral candidiasis [A] †	10/161 (6.21%)	8/155 (5.16%)	18/316 (5.7%)
Oral fungal infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Oral herpes [A] †	9/161 (5.59%)	4/155 (2.58%)	13/316 (4.11%)
Osteomyelitis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Otitis externa [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Parainfluenzae virus infection [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Paronychia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pharyngitis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Pharyngitis streptococcal [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pneumonia [A] †	14/161 (8.7%)	9/155 (5.81%)	23/316 (7.28%)
Pneumonia bacterial [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pneumonia fungal [A] †	5/161 (3.11%)	2/155 (1.29%)	7/316 (2.22%)
Pseudomonal bacteraemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pseudomonal sepsis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Pseudomonas infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pulmonary mycosis [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Respiratory syncytial virus infection [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Rhinitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Sepsis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Septic embolus [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Serratia bacteraemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Sinusitis [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Sinusitis fungal [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Skin candida [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Skin infection [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Staphylococcal bacteraemia [A] †	9/161 (5.59%)	15/155 (9.68%)	24/316 (7.59%)
Staphylococcal infection [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Staphylococcal scalded skin syndrome [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Staphylococcal sepsis [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Staphylococcal skin infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Stenotrophomonas infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Streptococcal bacteraemia [A] †	3/161 (1.86%)	4/155 (2.58%)	7/316 (2.22%)
Streptococcal sepsis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Subcutaneous abscess [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Tooth abscess [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)
Tooth infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Upper respiratory tract infection [A] †	2/161 (1.24%)	4/155 (2.58%)	6/316 (1.9%)
Urinary tract infection [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Urinary tract infection bacterial [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Urinary tract infection enterococcal [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Urinary tract infection pseudomonal [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Urinary tract infection staphylococcal [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Viral skin infection [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Vulvovaginal candidiasis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Injury, poisoning and procedural complications			
Anal injury [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bite [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Compression fracture [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Contusion [A] †	12/161 (7.45%)	17/155 (10.97%)	29/316 (9.18%)
Corneal abrasion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Eschar [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Excoriation [A] †	9/161 (5.59%)	3/155 (1.94%)	12/316 (3.8%)
Eye injury [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Face injury [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Fall [A] †	5/161 (3.11%)	1/155 (0.65%)	6/316 (1.9%)
Head injury [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Infusion related reaction [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Laceration [A] †	5/161 (3.11%)	5/155 (3.23%)	10/316 (3.16%)
Lip injury [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Muscle strain [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Nail avulsion [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Nail injury [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Overdose [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Periorbital haematoma [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Post procedural complication [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)
Post procedural haematoma [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Post procedural haematuria [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Post procedural haemorrhage [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Post procedural swelling [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Post-traumatic pain [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Procedural hypotension [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Procedural pain [A] †	12/161 (7.45%)	19/155 (12.26%)	31/316 (9.81%)
Procedural site reaction [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Refractoriness to platelet transfusion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Scratch [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Skin injury [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Spinal compression fracture [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Spinal fracture [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Subdural haematoma [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tongue injury [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tooth fracture [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Transfusion reaction [A] †	9/161 (5.59%)	7/155 (4.52%)	16/316 (5.06%)
Traumatic haematoma [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Urethral injury [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Wound [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Wound haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Wound secretion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Investigations			
Activated partial thromboplastin time prolonged [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Alanine aminotransferase increased [A] †	40/161 (24.84%)	13/155 (8.39%)	53/316 (16.77%)
Ammonia increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Aspartate aminotransferase increased [A] †	36/161 (22.36%)	8/155 (5.16%)	44/316 (13.92%)
Bacterial test [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bacterial test positive [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Blast cells present [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Blood albumin decreased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood alkaline phosphatase increased [A] †	11/161 (6.83%)	6/155 (3.87%)	17/316 (5.38%)
Blood amylase increased [A] †	9/161 (5.59%)	2/155 (1.29%)	11/316 (3.48%)
Blood beta-D-glucan increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Blood bicarbonate decreased [A] †	5/161 (3.11%)	0/155 (0%)	5/316 (1.58%)
Blood bicarbonate increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Blood bilirubin increased [A] †	12/161 (7.45%)	1/155 (0.65%)	13/316 (4.11%)
Blood calcium decreased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Blood chloride decreased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Blood chloride increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood creatinine increased [A] †	6/161 (3.73%)	3/155 (1.94%)	9/316 (2.85%)
Blood culture positive [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Blood glucose increased [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Blood iron increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Blood lactate dehydrogenase increased [A] †	9/161 (5.59%)	4/155 (2.58%)	13/316 (4.11%)
Blood magnesium decreased [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Blood magnesium increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood osmolarity increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood phosphorus decreased [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Blood phosphorus increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood potassium decreased [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Blood potassium increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Blood pressure increased [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Blood urea increased [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Blood uric acid increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Blood urine present [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Breath sounds abnormal [A] †	5/161 (3.11%)	7/155 (4.52%)	12/316 (3.8%)
Cardiac murmur [A] †	6/161 (3.73%)	9/155 (5.81%)	15/316 (4.75%)
Catheter culture positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Clostridium test positive [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Crystal urine present [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Culture stool positive [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Culture throat positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Culture urine positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cytomegalovirus test positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Diagnostic procedure [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Electrocardiogram PR shortened [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Electrocardiogram QT prolonged [A] †	4/161 (2.48%)	5/155 (3.23%)	9/316 (2.85%)
Electrocardiogram ST-T segment abnormal [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Electrocardiogram T wave abnormal [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Electrocardiogram abnormal [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Enterococcus test positive [A] †	5/161 (3.11%)	3/155 (1.94%)	8/316 (2.53%)
Escherichia test positive [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Fungal test positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gallop rhythm present [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Gamma-glutamyltransferase increased [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Glucose urine present [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Haematocrit decreased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Haemoglobin decreased [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Heart rate decreased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Heart rate increased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Hepatic enzyme increased [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
International normalised ratio increased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Lipase increased [A] †	10/161 (6.21%)	3/155 (1.94%)	13/316 (4.11%)
Liver function test abnormal [A] †	3/161 (1.86%)	7/155 (4.52%)	10/316 (3.16%)
Liver scan abnormal [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Lymph node palpable [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Monocyte count increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Neutrophil count decreased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Nitrite urine present [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Platelet count decreased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Protein total decreased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Protein total increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Protein urine present [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Prothrombin time prolonged [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Pulmonary function test decreased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
QRS axis abnormal [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Red blood cell count decreased [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Red blood cells urine positive [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Right ventricular systolic pressure increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Serum ferritin increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Spleen palpable [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Staphylococcus test positive [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Streptococcus test positive [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Total lung capacity decreased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Transaminases increased [A] †	10/161 (6.21%)	1/155 (0.65%)	11/316 (3.48%)
Troponin I increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Urinary sediment present [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Urine leukocyte esterase positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Urine output decreased [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Weight decreased [A] †	24/161 (14.91%)	11/155 (7.1%)	35/316 (11.08%)
Weight increased [A] †	13/161 (8.07%)	7/155 (4.52%)	20/316 (6.33%)
White blood cell count decreased [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
White blood cell count increased [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
White blood cells urine positive [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
pH urine increased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Metabolism and nutrition disorders			
Acidosis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Decreased appetite [A] †	57/161 (35.4%)	37/155 (23.87%)	94/316 (29.75%)
Dehydration [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Diabetes mellitus [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Fluid overload [A] †	22/161 (13.66%)	17/155 (10.97%)	39/316 (12.34%)
Fluid retention [A] †	9/161 (5.59%)	7/155 (4.52%)	16/316 (5.06%)
Folate deficiency [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Glucose tolerance impaired [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Gout [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Hyperamylasaemia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Hypercalcaemia [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Hyperglycaemia [A] †	17/161 (10.56%)	17/155 (10.97%)	34/316 (10.76%)
Hyperkalaemia [A] †	5/161 (3.11%)	1/155 (0.65%)	6/316 (1.9%)
Hyperlipasaemia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Hypermagnesaemia [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Hypernatraemia [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Hyperphosphataemia [A] †	7/161 (4.35%)	7/155 (4.52%)	14/316 (4.43%)
Hyperuricaemia [A] †	1/161 (0.62%)	3/155 (1.94%)	4/316 (1.27%)
Hypoalbuminaemia [A] †	22/161 (13.66%)	8/155 (5.16%)	30/316 (9.49%)
Hypocalcaemia [A] †	14/161 (8.7%)	5/155 (3.23%)	19/316 (6.01%)
Hypoglycaemia [A] †	5/161 (3.11%)	3/155 (1.94%)	8/316 (2.53%)
Hypokalaemia [A] †	61/161 (37.89%)	29/155 (18.71%)	90/316 (28.48%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hypomagnesaemia [A] †	26/161 (16.15%)	13/155 (8.39%)	39/316 (12.34%)
Hyponatraemia [A] †	15/161 (9.32%)	5/155 (3.23%)	20/316 (6.33%)
Hypophagia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hypophosphataemia [A] †	12/161 (7.45%)	7/155 (4.52%)	19/316 (6.01%)
Hypovolaemia [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Iron overload [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Malnutrition [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Metabolic acidosis [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Polydipsia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Tumour lysis syndrome [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Type 2 diabetes mellitus [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vitamin K deficiency [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] †	16/161 (9.94%)	7/155 (4.52%)	23/316 (7.28%)
Arthritis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Arthropathy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Back pain [A] †	29/161 (18.01%)	16/155 (10.32%)	45/316 (14.24%)
Bone loss [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Bone pain [A] †	4/161 (2.48%)	3/155 (1.94%)	7/316 (2.22%)
Bursitis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Chondritis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Coccydynia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Flank pain [A] †	4/161 (2.48%)	1/155 (0.65%)	5/316 (1.58%)
Groin pain [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Intervertebral disc degeneration [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Intervertebral disc protrusion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Joint effusion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Joint range of motion decreased [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Joint swelling [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Limb discomfort [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Muscle atrophy [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Muscle spasms [A] †	8/161 (4.97%)	5/155 (3.23%)	13/316 (4.11%)
Muscle tightness [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Muscular weakness [A] †	11/161 (6.83%)	1/155 (0.65%)	12/316 (3.8%)
Musculoskeletal chest pain [A] †	3/161 (1.86%)	6/155 (3.87%)	9/316 (2.85%)
Musculoskeletal discomfort [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Musculoskeletal pain [A] †	14/161 (8.7%)	9/155 (5.81%)	23/316 (7.28%)
Myalgia [A] †	9/161 (5.59%)	7/155 (4.52%)	16/316 (5.06%)
Myopathy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neck pain [A] †	5/161 (3.11%)	7/155 (4.52%)	12/316 (3.8%)
Osteoarthritis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Osteolysis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Osteoporosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Osteosclerosis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Pain in extremity [A] †	27/161 (16.77%)	12/155 (7.74%)	39/316 (12.34%)
Pain in jaw [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Rotator cuff syndrome [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Scoliosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Spinal column stenosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Spinal osteoarthritis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of eye [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Eye naevus [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Lip neoplasm malignant stage unspecified [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Lipoma [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Lung neoplasm [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Meningioma [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neoplasm malignant [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neurilemmoma [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Seborrhoeic keratosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nervous system disorders			
Amnesia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Apraxia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Ataxia [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Burning sensation [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Carotid arteriosclerosis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Central nervous system lesion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cerebral atrophy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cerebral haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cerebral infarction [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cerebral ischaemia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Cerebrovascular disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Convulsion [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Cranial nerve disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Depressed level of consciousness [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Dizziness [A] †	19/161 (11.8%)	28/155 (18.06%)	47/316 (14.87%)
Dizziness postural [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dysaesthesia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dysgeusia [A] †	10/161 (6.21%)	4/155 (2.58%)	14/316 (4.43%)
Dyskinesia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Encephalitis toxic [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Encephalopathy [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Headache [A] †	68/161 (42.24%)	44/155 (28.39%)	112/316 (35.44%)
Hemiparesis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hepatic encephalopathy [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hyperaesthesia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hypoaesthesia [A] †	3/161 (1.86%)	4/155 (2.58%)	7/316 (2.22%)
Hypogeusia [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hypokinesia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Hyporeflexia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Intention tremor [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Lethargy [A] †	3/161 (1.86%)	4/155 (2.58%)	7/316 (2.22%)
Loss of consciousness [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Memory impairment [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Migraine [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Myoclonus [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Neuropathy peripheral [A] †	4/161 (2.48%)	2/155 (1.29%)	6/316 (1.9%)
Nystagmus [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Paraesthesia [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Peroneal nerve palsy [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Polyneuropathy [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Presyncope [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Restless legs syndrome [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Sciatica [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Sensory disturbance [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Sinus headache [A] †	3/161 (1.86%)	4/155 (2.58%)	7/316 (2.22%)
Slow speech [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Somnolence [A] †	9/161 (5.59%)	7/155 (4.52%)	16/316 (5.06%)
Speech disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Syncope [A] †	6/161 (3.73%)	4/155 (2.58%)	10/316 (3.16%)
Tension headache [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Tremor [A] †	9/161 (5.59%)	7/155 (4.52%)	16/316 (5.06%)
Psychiatric disorders			
Aggression [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Agitation [A] †	9/161 (5.59%)	2/155 (1.29%)	11/316 (3.48%)
Anger [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Anxiety [A] †	35/161 (21.74%)	20/155 (12.9%)	55/316 (17.41%)
Confusional state [A] †	30/161 (18.63%)	13/155 (8.39%)	43/316 (13.61%)
Delirium [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Depressed mood [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Depression [A] †	20/161 (12.42%)	8/155 (5.16%)	28/316 (8.86%)
Disorientation [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Dysphoria [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Fear [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Flat affect [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Hallucination [A] †	3/161 (1.86%)	3/155 (1.94%)	6/316 (1.9%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hallucination, visual [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Insomnia [A] †	51/161 (31.68%)	42/155 (27.1%)	93/316 (29.43%)
Mental status changes [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Mood altered [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nightmare [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Panic attack [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Restlessness [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Renal and urinary disorders			
Bladder dilatation [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bladder mass [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Bladder spasm [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Chromaturia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dysuria [A] †	8/161 (4.97%)	3/155 (1.94%)	11/316 (3.48%)
Enuresis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Haematuria [A] †	8/161 (4.97%)	11/155 (7.1%)	19/316 (6.01%)
Incontinence [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Kidney enlargement [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nephrolithiasis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Nocturia [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Oliguria [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pollakiuria [A] †	5/161 (3.11%)	6/155 (3.87%)	11/316 (3.48%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Polyuria [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Proteinuria [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Renal cyst [A] †	4/161 (2.48%)	4/155 (2.58%)	8/316 (2.53%)
Renal disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Renal failure [A] †	4/161 (2.48%)	4/155 (2.58%)	8/316 (2.53%)
Renal failure acute [A] †	5/161 (3.11%)	2/155 (1.29%)	7/316 (2.22%)
Renal failure chronic [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Renal tubular necrosis [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Urethritis noninfective [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Urinary incontinence [A] †	9/161 (5.59%)	6/155 (3.87%)	15/316 (4.75%)
Urinary retention [A] †	1/161 (0.62%)	9/155 (5.81%)	10/316 (3.16%)
Urine abnormality [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Urine flow decreased [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Reproductive system and breast disorders			
Balanitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Breast haematoma [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Breast pain [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Gynaecomastia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ovarian cyst [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pelvic pain [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Penile blister [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Penile haemorrhage [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Penile pain [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Prostatomegaly [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Scrotal oedema [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Testicular pain [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vaginal haemorrhage [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Vulvovaginal rash [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vulvovaginal swelling [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Acute respiratory failure [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Asthma [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Atelectasis [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Bronchial wall thickening [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Bronchospasm [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Chronic obstructive pulmonary disease [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Cough [A] †	34/161 (21.12%)	26/155 (16.77%)	60/316 (18.99%)
Dry throat [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dysphonia [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Dyspnoea [A] †	30/161 (18.63%)	18/155 (11.61%)	48/316 (15.19%)
Dyspnoea exertional [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Epistaxis [A] †	30/161 (18.63%)	19/155 (12.26%)	49/316 (15.51%)
Haemoptysis [A] †	6/161 (3.73%)	10/155 (6.45%)	16/316 (5.06%)
Hiccups [A] †	9/161 (5.59%)	2/155 (1.29%)	11/316 (3.48%)
Hypoxia [A] †	9/161 (5.59%)	3/155 (1.94%)	12/316 (3.8%)
Increased bronchial secretion [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Interstitial lung disease [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Laryngospasm [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Lung infiltration [A] †	8/161 (4.97%)	4/155 (2.58%)	12/316 (3.8%)
Nasal congestion [A] †	7/161 (4.35%)	3/155 (1.94%)	10/316 (3.16%)
Nasal dryness [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Nasal mucosal disorder [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Nasal ulcer [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Oropharyngeal blistering [A] †	3/161 (1.86%)	3/155 (1.94%)	6/316 (1.9%)
Oropharyngeal pain [A] †	10/161 (6.21%)	11/155 (7.1%)	21/316 (6.65%)
Oropharyngeal plaque [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Orthopnoea [A] †	1/161 (0.62%)	2/155 (1.29%)	3/316 (0.95%)
Paranasal cyst [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Paranasal sinus hypersecretion [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pharyngeal erythema [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Pharyngeal inflammation [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pleural effusion [A] †	16/161 (9.94%)	15/155 (9.68%)	31/316 (9.81%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pleuritic pain [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Pneumonitis [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)
Pneumothorax [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Productive cough [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Pulmonary alveolar haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pulmonary congestion [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)
Pulmonary fibrosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pulmonary haemorrhage [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Pulmonary hypertension [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Pulmonary oedema [A] †	8/161 (4.97%)	2/155 (1.29%)	10/316 (3.16%)
Rales [A] †	9/161 (5.59%)	9/155 (5.81%)	18/316 (5.7%)
Respiratory alkalosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Respiratory distress [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Respiratory failure [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Respiratory tract congestion [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Rhinalgia [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Rhinitis allergic [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Rhinorrhoea [A] †	3/161 (1.86%)	3/155 (1.94%)	6/316 (1.9%)
Rhonchi [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Sinus congestion [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Sleep apnoea syndrome [A] †	0/161 (0%)	3/155 (1.94%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Sputum discoloured [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Stridor [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Tachypnoea [A] †	1/161 (0.62%)	5/155 (3.23%)	6/316 (1.9%)
Throat lesion [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Upper-airway cough syndrome [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Vocal cord polyp [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Wheezing [A] †	7/161 (4.35%)	2/155 (1.29%)	9/316 (2.85%)
Skin and subcutaneous tissue disorders			
Actinic keratosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Alopecia [A] †	14/161 (8.7%)	3/155 (1.94%)	17/316 (5.38%)
Blister [A] †	7/161 (4.35%)	3/155 (1.94%)	10/316 (3.16%)
Blood blister [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Decubitus ulcer [A] †	8/161 (4.97%)	1/155 (0.65%)	9/316 (2.85%)
Dermal cyst [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Dermatitis [A] †	1/161 (0.62%)	3/155 (1.94%)	4/316 (1.27%)
Dermatitis allergic [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Drug eruption [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Dry skin [A] †	24/161 (14.91%)	13/155 (8.39%)	37/316 (11.71%)
Ecchymosis [A] †	9/161 (5.59%)	20/155 (12.9%)	29/316 (9.18%)
Erythema [A] †	19/161 (11.8%)	22/155 (14.19%)	41/316 (12.97%)
Exfoliative rash [A] †	6/161 (3.73%)	2/155 (1.29%)	8/316 (2.53%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Generalised erythema [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Heat rash [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Hidradenitis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Hyperhidrosis [A] †	12/161 (7.45%)	6/155 (3.87%)	18/316 (5.7%)
Hyperkeratosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Increased tendency to bruise [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Ingrowing nail [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Lentigo [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Leukocytoclastic vasculitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nail disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Nail dystrophy [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Night sweats [A] †	5/161 (3.11%)	10/155 (6.45%)	15/316 (4.75%)
Pain of skin [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Palmar erythema [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Palmar-plantar erythrodysaesthesia syndrome [A] †	30/161 (18.63%)	2/155 (1.29%)	32/316 (10.13%)
Papule [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pemphigoid [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Petechiae [A] †	22/161 (13.66%)	24/155 (15.48%)	46/316 (14.56%)
Photodermatosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pigmentation disorder [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Pruritus [A] †	19/161 (11.8%)	5/155 (3.23%)	24/316 (7.59%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pruritus generalised [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Purpura [A] †	2/161 (1.24%)	3/155 (1.94%)	5/316 (1.58%)
Rash [A] †	40/161 (24.84%)	22/155 (14.19%)	62/316 (19.62%)
Rash erythematous [A] †	14/161 (8.7%)	3/155 (1.94%)	17/316 (5.38%)
Rash follicular [A] †	3/161 (1.86%)	0/155 (0%)	3/316 (0.95%)
Rash generalised [A] †	17/161 (10.56%)	7/155 (4.52%)	24/316 (7.59%)
Rash macular [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Rash maculo-papular [A] †	4/161 (2.48%)	4/155 (2.58%)	8/316 (2.53%)
Rash papular [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Rash pruritic [A] †	6/161 (3.73%)	1/155 (0.65%)	7/316 (2.22%)
Rash vesicular [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Rosacea [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Scab [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Skin discolouration [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Skin disorder [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Skin exfoliation [A] †	23/161 (14.29%)	3/155 (1.94%)	26/316 (8.23%)
Skin haemorrhage [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Skin hyperpigmentation [A] †	2/161 (1.24%)	2/155 (1.29%)	4/316 (1.27%)
Skin lesion [A] †	5/161 (3.11%)	8/155 (5.16%)	13/316 (4.11%)
Skin mass [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)
Skin ulcer [A] †	2/161 (1.24%)	0/155 (0%)	2/316 (0.63%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Stasis dermatitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Subcutaneous nodule [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Swelling face [A] †	1/161 (0.62%)	4/155 (2.58%)	5/316 (1.58%)
Toxic skin eruption [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Urticaria [A] †	2/161 (1.24%)	5/155 (3.23%)	7/316 (2.22%)
Social circumstances			
Andropause [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vascular disorders			
Aortic aneurysm [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Aortic arteriosclerosis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Aortic calcification [A] †	0/161 (0%)	2/155 (1.29%)	2/316 (0.63%)
Aortic disorder [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Arteriosclerosis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Deep vein thrombosis [A] †	6/161 (3.73%)	3/155 (1.94%)	9/316 (2.85%)
Flushing [A] †	19/161 (11.8%)	11/155 (7.1%)	30/316 (9.49%)
Haematoma [A] †	4/161 (2.48%)	3/155 (1.94%)	7/316 (2.22%)
Hot flush [A] †	3/161 (1.86%)	2/155 (1.29%)	5/316 (1.58%)
Hypertension [A] †	29/161 (18.01%)	21/155 (13.55%)	50/316 (15.82%)
Hypotension [A] †	37/161 (22.98%)	33/155 (21.29%)	70/316 (22.15%)
Infarction [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Jugular vein distension [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Jugular vein thrombosis [A] †	2/161 (1.24%)	1/155 (0.65%)	3/316 (0.95%)

	Clofarabine (IV Formulation) and Cytarabine	Placebo and Cytarabine	Overall
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lymphoedema [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Orthostatic hypotension [A] †	9/161 (5.59%)	4/155 (2.58%)	13/316 (4.11%)
Pallor [A] †	2/161 (1.24%)	9/155 (5.81%)	11/316 (3.48%)
Subclavian vein thrombosis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Thrombosis [A] †	3/161 (1.86%)	1/155 (0.65%)	4/316 (1.27%)
Vascular stenosis [A] †	0/161 (0%)	1/155 (0.65%)	1/316 (0.32%)
Vasculitis [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Vena cava thrombosis [A] †	1/161 (0.62%)	1/155 (0.65%)	2/316 (0.63%)
Venous insufficiency [A] †	1/161 (0.62%)	0/155 (0%)	1/316 (0.32%)
Venous thrombosis limb [A] †	1/161 (0.62%)	3/155 (1.94%)	4/316 (1.27%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 14.1

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

In multi-site studies, PI can publish after Genzyme publishes or 18 months after study completion. PI gives Genzyme a draft 60 days before publication. Genzyme can ask that confidential information be removed, and can defer publication another 60 days upon notifying PI that it will file a patent application on inventions contained in the draft.

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