# Clinical trial results:
# Open-label, Single-arm Trial to Evaluate Antitumor Activity, Safety, and Pharmacokinetics of Isatuximab Used in Combination With Chemotherapy in Pediatric Patients From 28 Days to Less Than 18 Years of Age With Relapsed/Refractory B or T Acute Lymphoblastic Leukemia or Acute Myeloid Leukemia In First or Second Relapse

## Summary

| | |
|---|---|
| EudraCT number | 2018-002697-45 |
| Trial protocol | SE NO FI DK FR NL PT BE DE CZ GR Outside EU/EEA IT |
| Global end of trial date | 26 May 2023 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 02 December 2023 |
| First version publication date | 02 December 2023 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | ACT15378 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03860844 |
| WHO universal trial number (UTN) | U1111-1202-1096 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Sanofi aventis recherche & développement |
| Sponsor organisation address | 1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-002205-PIP01-17 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 26 May 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 26 May 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the anti-leukemic activity of isatuximab in combination with chemotherapies in pediatric participants of 28 days to less than 18 years of age with Relapsed/Refractory (R/R) Acute Lymphoblastic Leukemia (ALL) or Acute Myeloid Leukemia (AML).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric participants. The parent (s) or guardian (s) as well as children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 06 August 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Mexico: 3 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Norway: 3 |
| Country: Number of subjects enrolled | Peru: 2 |
| Country: Number of subjects enrolled | Portugal: 4 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | United States: 2 |
| Country: Number of subjects enrolled | Denmark: 4 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | Germany: 2 |
| Country: Number of subjects enrolled | Greece: 2 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Italy: 7 |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Argentina: 7 |
| Country: Number of subjects enrolled | Brazil: 12 |

| | |
|---|---|
| Worldwide total number of subjects | 67 |
| EEA total number of subjects | 36 |

Notes:

| **Subjects enrolled per age group** | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 1 |
| Children (2-11 years) | 48 |
| Adolescents (12-17 years) | 18 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This Phase II, open-label, single-arm study was conducted in 3 separate cohorts at 41 investigational sites in 16 countries. A total of 67 participants were enrolled between 06 Aug 2019 and 08 Jun 2022.

### Pre-assignment

Screening details:

The study consisted of a screening period (up to 3 weeks prior to the first study treatment administration), treatment period (Day 1 to Day 57 for ALL; Day 1 to Day 22 for AML), a period of aplasia followed by recovery period; an end of treatment (EOT) visit within 30 days after hematological recovery and follow-up period.

### Period 1

| | |
|---|---|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | B-cell Acute Lymphoblastic Leukemia (B-ALL) |

Arm description:

Participants with B-ALL received isatuximab 20 milligram per kilogram (mg/kg) intravenous (IV) infusion once every week (QW) for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and every 2 weeks (Q2W) during the consolidation period (i.e., on Days 29, 43, and 57). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Isatuximab |
| Investigational medicinal product code | SAR650984 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Isatuximab was administered as 20 mg/kg weekly on Days 1, 8, 15, 22, 29, 43, and 57.

| | |
|---|---|
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Dexamethasone was administered before each administration of isatuximab, at least 15 to 30 minutes (but no longer than 60 minutes) prior to infusion as premedication for prevention of infusion associated reactions consisting of dexamethasone 10 mg/meter square (m^2) (maximum 20 mg) IV or orally (PO) on Days -3, -2, and -1 before isatuximab administration, Days 1, 8, 15 to 19, 22, and 29 to 33 during the induction period, and on Days 43 to 47 and 57 during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Mitoxantrone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |

| | |
|---|---|
| Routes of administration | Intravenous use |

Dosage and administration details:

Mitoxantrone was administered as 10 mg/m^2 IV over 15 minutes on Days 8 and 9 of the induction period.

| | |
|---|---|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Doxorubicin was administered as 25 mg/m^2 IV over 15 minutes on Days 10, 17, 24, and 31 of the induction period.

| | |
|---|---|
| Investigational medicinal product name | Vincristine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Vincristine was administered as 1.5 mg/m^2 IV on Days 10, 17, 24, and 31 during the induction period (not exceeding 2 mg per infusion in any participant) and on Day 38 during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Pegaspargase |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use, Intravenous use |

Dosage and administration details:

Pegaspargase was administered as 1000 International units (IU)/m^2 on Days 10 and 24 during the induction period and Day 44 during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | L-asparaginase |
| Investigational medicinal product code | |
| Other name | Erwinase |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use, Intravenous use |

Dosage and administration details:

L-asparaginase was administered as 25000 IU/m^2 on Days 8, 10, 12, 15, 17, 19, 22, 24, 26, 29, 31, 33 during induction and days 43, 45, 47, 50, 52, 54 during consolidation, only in case of confirmed hypersensitivity reaction to pegaspargase prior or during the study or loss of asparaginase activity and/or country availability and regulations.

| | |
|---|---|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cyclophosphamide 440 mg/m^2 was administered as a 1-hour infusion on Days 50 to 54 (inclusive) during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Etoposide 100 mg/m^2 was administered as a 2-hour infusion on Days 50 to 54 (inclusive) during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Methotrexate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Methotrexate 1000 mg/m^2 was infused over 36 hours and calcium folinate rescue started 48 hours from start of infusion on Day 43 during the consolidation period.

| | |
|---|---|
| **Arm title** | T-cell Acute Lymphoblastic Leukemia (T-ALL) |

Arm description:

Participants with T-ALL received isatuximab 20 mg/kg IV infusion QW for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and Q2W during the consolidation period (i.e., on Days 29, 43, and 57. Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Isatuximab |
| Investigational medicinal product code | SAR650984 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Isatuximab was administered as 20 mg/kg weekly on Days 1, 8, 15, 22, 29, 43, and 57.

| | |
|---|---|
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Dexamethasone was administered before each administration of isatuximab, at least 15 to 30 minutes (but no longer than 60 minutes) prior to infusion as premedication for prevention of infusion associated reactions consisting of dexamethasone 10 mg/m^2 (maximum 20 mg) IV or PO on Days -3, -2, and -1 before isatuximab administration, Days 1, 8, 15 to 19, 22, and 29 to 33 during the induction period, and on Days 43 to 47 and 57 during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Mitoxantrone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Mitoxantrone was administered as 10 mg/m^2 IV over 15 minutes on Days 8 and 9 of the induction period.

| | |
|---|---|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Doxorubicin was administered as 25 mg/m^2 IV over 15 minutes on Days 10, 17, 24, and 31 of the induction period.

| | |
|---|---|
| Investigational medicinal product name | Vincristine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Vincristine was administered as 1.5 mg/m^2 IV on Days 10, 17, 24, and 31 during the induction period (not exceeding 2 mg per infusion in any participant) and on Day 38 during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Pegaspargase |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use, Intravenous use |

Dosage and administration details:

Pegaspargase was administered as 1000 IU/m^2 on Days 10 and 24 during the induction period and Day 44 during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | L-asparaginase |
| Investigational medicinal product code | |
| Other name | Erwinase |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use, Intravenous use |

Dosage and administration details:

L-asparaginase was administered as 25000 IU/m^2 on Days 8, 10, 12, 15, 17, 19, 22, 24, 26, 29, 31, 33 during induction and days 43, 45, 47, 50, 52, 54 during consolidation, only in case of confirmed hypersensitivity reaction to pegaspargase prior or during the study or loss of asparaginase activity and/or country availability and regulations.

| | |
|---|---|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cyclophosphamide 440 mg/m^2 was administered as a 1-hour infusion on Days 50 to 54 (inclusive) during the consolidation period.

| | |
|---|---|
| Investigational medicinal product name | Methotrexate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Methotrexate 1000 mg/m^2 was infused over 36 hours and calcium folinate rescue started 48 hours from start of infusion on Day 43 during the consolidation period.

| | |
|---|---|
| **Arm title** | Acute Myeloid Leukemia (AML) |

Arm description:

Participants with AML received isatuximab 20 mg/kg IV infusion on Days 1, 8, and 15 of each Cycle (up to 2 treatment cycles, each cycle 28 days). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Isatuximab |
| Investigational medicinal product code | SAR650984 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Isatuximab was administered as 20 mg/kg weekly on Days 1, 8, 15 (mandatory for Cycles 1 and 2).

| | |
|---|---|
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet, Solution for injection |
| Routes of administration | Oral use, Intravenous use |

Dosage and administration details:

Dexamethasone was administered as a premedication for prevention of infusion associated reactions before each administration of isatuximab, at least 15 to 30 minutes (but no longer than 60 minutes) prior to infusion consisting of dexamethasone 10 mg/m^2 (maximum 20 mg) IV or PO on Days 1, 8, and 15 during the induction period (mandatory for Cycle 1 and before first isatuximab infusion Cycle 2). It was optionally used for rapid control of tumor burden on Days -3, -2 and -1. When dexamethasone was administered at 10 mg/m^2 orally, it could have been divided in 2 daily doses.

| | |
|---|---|
| Investigational medicinal product name | Fludarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Fludarabine 30 mg/m^2 IV was administered as 30-minute infusion after granulocyte colony-stimulating factor (G-CSF) administration, if any on Days 8 to 12 (inclusive) (mandatory for Cycles 1 and 2).

| | |
|---|---|
| Investigational medicinal product name | Cytarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cytarabine 2 gram (g)/m^2 was administered as a 4-hour infusion, beginning 4 hours after start of fludarabine on Days 8 to 12 (inclusive) (mandatory for Cycles 1 and 2)

| | |
|---|---|
| Investigational medicinal product name | Anthracycline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Anthracycline (a choice of liposomal daunorubicin 60 mg/m^2, non-liposomal daunorubicin 60 mg/m^2, or idarubicin 10 mg/m^2) was given after administration of fludarabine. Anthracycline administration on Day 8 in Cycle 1 was mandatory. Administrations on Cycle 1 Days 10 and 12 and on Cycle 2 were at the Investigator’s discretion.

| | |
|---|---|
| Investigational medicinal product name | Filgrastim |
| Investigational medicinal product code | |
| Other name | Granulocyte colony-stimulating factor |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use, Subcutaneous use |

Dosage and administration details:

Filgrastim (optional for Cycles 1 and 2) was administered as 200 microgram/m^2/day on Days 7 to 12 (inclusive) and was continued until neutrophil recovery.

| **Number of subjects in period 1** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) |
|---|---|---|---|
| Started | 27 | 13 | 27 |
| Completed | 19 | 7 | 20 |
| Not completed | 8 | 6 | 7 |
| Other, Not related to COVID-19 | - | 1 | - |
| Adverse event, unrelated to Coronavirus Disease-19 | 3 | 2 | 3 |
| Progressive disease | 5 | 3 | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | B-cell Acute Lymphoblastic Leukemia (B-ALL) |

Reporting group description:

Participants with B-ALL received isatuximab 20 milligram per kilogram (mg/kg) intravenous (IV) infusion once every week (QW) for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and every 2 weeks (Q2W) during the consolidation period (i.e., on Days 29, 43, and 57). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| Reporting group title | T-cell Acute Lymphoblastic Leukemia (T-ALL) |
|---|---|

Reporting group description:

Participants with T-ALL received isatuximab 20 mg/kg IV infusion QW for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and Q2W during the consolidation period (i.e., on Days 29, 43, and 57. Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| Reporting group title | Acute Myeloid Leukemia (AML) |
|---|---|

Reporting group description:

Participants with AML received isatuximab 20 mg/kg IV infusion on Days 1, 8, and 15 of each Cycle (up to 2 treatment cycles, each cycle 28 days). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| Reporting group values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) |
|---|---|---|---|
| Number of subjects | 27 | 13 | 27 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 8.22 | 8.72 | 9.04 |
| standard deviation | ± 3.92 | ± 4.15 | ± 5.41 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 10 | 4 | 12 |
| Male | 17 | 9 | 15 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 3 | 0 | 0 |
| Asian | 1 | 1 | 4 |

| | | | |
|---|---|---|---|
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 1 | 2 |
| White | 17 | 7 | 15 |
| More than one race | 1 | 0 | 0 |
| Unknown or Not Reported | 4 | 4 | 6 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 67 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 26 | | |
| Male | 41 | | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 3 | | |
| Asian | 6 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 4 | | |
| White | 39 | | |
| More than one race | 1 | | |
| Unknown or Not Reported | 14 | | |

## End points

### End points reporting groups

| Reporting group title | B-cell Acute Lymphoblastic Leukemia (B-ALL) |
|---|---|

Reporting group description:

Participants with B-ALL received isatuximab 20 milligram per kilogram (mg/kg) intravenous (IV) infusion once every week (QW) for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and every 2 weeks (Q2W) during the consolidation period (i.e., on Days 29, 43, and 57). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| Reporting group title | T-cell Acute Lymphoblastic Leukemia (T-ALL) |
|---|---|

Reporting group description:

Participants with T-ALL received isatuximab 20 mg/kg IV infusion QW for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and Q2W during the consolidation period (i.e., on Days 29, 43, and 57. Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| Reporting group title | Acute Myeloid Leukemia (AML) |
|---|---|

Reporting group description:

Participants with AML received isatuximab 20 mg/kg IV infusion on Days 1, 8, and 15 of each Cycle (up to 2 treatment cycles, each cycle 28 days). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

### Primary: Percentage of Participants With Complete Response (CR) Rate

| End point title | Percentage of Participants With Complete Response (CR) |
|---|---|

End point description:

The CR rate (CR+CRi [CR with incomplete peripheral recovery]): % of participants achieving CR assessed by investigator per National Comprehensive Cancer Network (NCCN) guidelines version 1.2018 criteria. CR:<5% blasts in bone marrow aspirate (BMA)with spicules;no circulating blasts(ALL)/no blasts with Auer rods(AML)or extramedullary disease,no lymphadenopathy, splenomegaly,skin/gum infiltration/testicular mass/central nervous system involvement(ALL),trilineage hematopoiesis(ALL);Absolute neutrophil count(ANC)>=1000/microliter (mcL);platelets >100000/mcL;red blood cell transfusion independence.If physician documented transfusion dependency related to study treatment;not participant’s underlying disease, CRi was reported.CRi=CR, except neutrophils (<1000/mcL) and/or platelets recovery(<100000/mcL). Evaluable population(EP):Evaluable participants from All-treated (AT) population who received atleast 1 full dose of isatuximab in Cycle 1 and who had atleast 1 valid response value evaluable

| End point type | Primary |
|---|---|

End point timeframe:

From enrollment until the primary analysis completion date of 12 Sep 2022; the median duration of exposure was approximately 7 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

| **End point values** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 11 | 23 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 52.0 | 45.5 | 60.9 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) |
|---|---|

End point description:

An AE was defined as any untoward medical occurrence in a participant temporally associated with the use of study treatment, whether or not considered related to the study treatment. SAEs were any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. TEAEs were defined as an AE which occurred after the first dose of study treatment administration until the last dose plus 30 days, or until the start of hematological recovery period or a new anti-leukemia/lymphoma therapy, whichever occurred first. The AT population consisted of all participants who received at least 1 dose (even incomplete) of study treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

From the time of the first treatment administration (Day 1) up to 30 days after the last treatment (maximum duration of exposure of 13.1 weeks for B-ALL cohort, 10.7 weeks for T-ALL cohort and 7.1 weeks for AML cohort)

| **End point values** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 27 | 13 | 27 | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Any TEAEs | 27 | 13 | 26 | |
| Any TESAEs | 19 | 12 | 17 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Infusion Reactions (IRs)

| End point title | Number of Participants With Infusion Reactions (IRs) |
|---|---|

End point description:

An IR was an AE related to isatuximab typically with onset within 24 hours from the start of the isatuximab infusion and was reported by the investigator. The AT population consisted of all participants who received at least 1 dose (even incomplete) of study treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

From the time of the first treatment administration (Day 1) up to 30 days after the last treatment (maximum duration of exposure of 13.1 weeks for B-ALL cohort, 10.7 weeks for T-ALL cohort and 7.1 weeks for AML cohort)

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 27 | 13 | 27 | |
| Units: participants | | | | |
| number (not applicable) | 9 | 5 | 15 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: B-ALL and T-ALL: Area Under the Concentration Time Curve (AUC) of Isatuximab

| End point title | B-ALL and T-ALL: Area Under the Concentration Time Curve (AUC) of Isatuximab[2] |
|---|---|

End point description:

Plasma samples were collected at specified timepoints to determine the AUC of isatuximab. The Pharmacokinetic (PK) population consisted of all participants from the AT population with at least 1 PK parameter available (isatuximab concentration). Only those participants with data available at specified timepoints were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 0 to Week 1, Week 0 to Week 5, and Week 0 to Week 10

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from B-ALL and T-ALL cohort were included in this endpoint.

| **End point values** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 12 | | |
| Units: mg*hour (h)/Liter (L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 to Week 1 | 31703 (± 10048) | 29057 (± 8294) | | |
| Week 0 to Week 5 | 299071 (± 127581) | 289167 (± 93095) | | |
| Week 0 to Week 10 | 582686 (± 316749) | 540375 (± 233411) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: AML: AUC of Isatuximab

| End point title | AML: AUC of Isatuximab[3] |
|---|---|

End point description:

Plasma samples were collected at specified timepoints to determine the AUC of isatuximab. The PK population consisted of all participants from the AT population with at least 1 PK parameter available (isatuximab concentration). Only those participants with data available at specified timepoints were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 0 to Week 1, Week 0 to Week 3, and Week 0 to Week 8

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from AML cohort were included in this endpoint.

| **End point values** | Acute Myeloid Leukemia (AML) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: mg*h/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 to Week 1 | 28592 (± 6858) | | | |
| Week 0 to Week 3 | 130862 (± 40827) | | | |
| Week 0 to Week 8 | 291962 (± 112222) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: B-ALL and T-ALL: Plasma Concentration Reached by Isatuximab Before Next Dose Administration (Ctrough)

| End point title | B-ALL and T-ALL: Plasma Concentration Reached by Isatuximab Before Next Dose Administration (Ctrough)[4] |
|---|---|

End point description:

Plasma samples were collected at specified timepoints to determine the Ctrough of isatuximab. The PK population consisted of all participants from the AT population with at least 1 PK parameter available (isatuximab concentration). Only those participants with data available at specified timepoints were analyzed and are denoted by 'n' in the categories. 99999= Standard deviation (SD) could not be derived for a single participant.

| End point type | Secondary |
|---|---|

End point timeframe:

Cycle 1 Day 8, Cycle 1 Day 15, Cycle 1 Day 22, Cycle 1 Day 29, Cycle 2 Day 43, Cycle 2 Day 57

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from B-ALL and T-ALL cohort were included in this endpoint.

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 13 | | |
| Units: microgram/milliliter (mcg/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1: Day 8 (n=25, 11) | 114 (± 45.7) | 127 (± 49.9) | | |
| Cycle 1: Day 15 (n=23, 11) | 272 (± 118) | 263 (± 103) | | |
| Cycle 1: Day 22 (n=15, 8) | 388 (± 163) | 323 (± 206) | | |
| Cycle 1: Day 29 (n=18, 9) | 475 (± 174) | 426 (± 209) | | |
| Cycle 2: Day 43 (n=5, 1) | 504 (± 296) | 357 (± 99999) | | |
| Cycle 2: Day 57 (n=8, 2) | 531 (± 224) | 478 (± 261) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: AML: Plasma Concentration Reached by Isatuximab Before Next Dose Administration (Ctrough)

| End point title | AML: Plasma Concentration Reached by Isatuximab Before Next Dose Administration (Ctrough)[5] |
|---|---|

End point description:

Plasma samples were collected at specified timepoints to determine the Ctrough of isatuximab. The PK population consisted of all participants from the AT population with at least 1 PK parameter available (isatuximab concentration). Only those participants with data available at specified timepoints were analyzed and are denoted by 'n' in the categories.

| End point type | Secondary |
|---|---|

End point timeframe:

Cycle 1 Day 8, Cycle 1 Day 15, Cycle 2 Day 1 and Cycle 2 Day 15

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from AML cohort were included in this endpoint.

| **End point values** | Acute Myeloid Leukemia (AML) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1: Day 8 (n=19) | 126 (± 41.0) | | | |
| Cycle 1: Day 15 (n=24) | 217 (± 60.6) | | | |
| Cycle 2: Day 1 (n=10) | 115 (± 94.2) | | | |
| Cycle 2: Day 15 (n=8) | 420 (± 205) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: B-ALL and T-ALL: Concentrations at the End of Infusion (Ceoi) of Isatuximab

| End point title | B-ALL and T-ALL: Concentrations at the End of Infusion (Ceoi) of Isatuximab[6] |
|---|---|

End point description:

Ceoi is the plasma concentration observed at the end of intravenous infusion of isatuximab. The PK population consisted of all participants from the AT population with at least 1 PK parameter available (isatuximab concentration). Only those participants with data available at specified timepoints were analyzed and are denoted by 'n' in the categories.

| End point type | Secondary |
|---|---|

End point timeframe:

At end of infusion on Cycle 1 Days 1 and 29

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from B-ALL and T-ALL cohort were included in this endpoint.

| **End point values** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 13 | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---|---|---|---|
| Cycle 1: Day 1 (n=21, 8) | 452 (± 344) | 259 (± 120) | | |
| Cycle 1: Day 29 (n=19, 7) | 835 (± 366) | 745 (± 330) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: AML: Ceoi of Isatuximab

| End point title | AML: Ceoi of Isatuximab[7] |
|---|---|

End point description:

Ceoi is the plasma concentration observed at the end of intravenous infusion of isatuximab. The PK population consisted of all participants from the AT population with at least 1 PK parameter available (isatuximab concentration). Only those participants with data available at specified timepoints were analyzed and are denoted by 'n' in the categories.

| End point type | Secondary |
|---|---|

End point timeframe:

At end of infusion on Cycle 1 Days 1 and 15

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from AML cohort were included in this endpoint.

| End point values | Acute Myeloid Leukemia (AML) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1: Day 1 (n=19) | 363 (± 110) | | | |
| Cycle 1: Day 15 (n=20) | 562 (± 176) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Negative Minimal Residual Disease (MRD)

| End point title | Number of Participants With Negative Minimal Residual Disease (MRD) |
|---|---|

End point description:

The MRD assessment was performed by next generation sequencing using clonoSEQ and T-cell receptor assays for B-ALL and T-ALL cohorts respectively. It was performed by flow cytometry for AML cohort. Number of participants with CR or CRi who achieved negative MRD in bone marrow and blood were analyzed. The EP consisted of evaluable participants from the AT population who received at least 1 full dose of isatuximab in Cycle 1 and who had at least 1 valid response value that was evaluable. Only those participants who achieved CR/CRi were analyzed. 9999 = In AML indication, peripheral blood tissue is not representative of the tumor burden and cannot be used to assess MRD.

| End point type | Secondary |
|---|---|

End point timeframe:

From screening until the study end date, approximately 45 months

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 5 | 14 | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Blood, 1 in 10^6 | 3 | 1 | 9999 | |
| Bone marrow, 1 in 10^6 | 0 | 2 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Response Rate (ORR)

| End point title | Overall Response Rate (ORR) |
|---|---|

End point description:

ORR:Percentage of participants with CR/CRi or partial response for blood and bone marrow disease based on NCCN guideline. CR: <5% blasts in BMA with spicules; no circulating blasts (ALL)/no blasts with Auer rods (AML) or extramedullary disease, no lymphadenopathy, splenomegaly, skin/gum infiltration/testicular mass/central nervous system involvement (ALL), trilineage hematopoiesis (ALL);ANC >=1000/mcL; platelets >100000/mcL; RBC transfusion independence. If physician documented transfusion dependency related to study treatment;not to participant's underlying disease, CRi was reported. CRi met the same criteria as CR, except neutrophils and/or platelets recovery (ANC <1000/mcL or platelets <100000/mcL). PR: >50% decrease in the sum of the product of the greatest perpendicular diameters of the mediastinal enlargement. For participants with a previous positive positron emission tomography (PET) scan, a post-treatment PET was to be positive in at least 1 previously involved site. The EP.

| End point type | Secondary |
|---|---|

End point timeframe:

From enrollment until the primary analysis completion date of 12 Sep 2022; the median duration of exposure was approximately 7 weeks

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 11 | 23 | |
| Units: percentage of participants | | | | |
| number (confidence interval 80%) | 52.0 (37.5 to 66.2) | 54.5 (31.8 to 75.9) | 65.2 (49.7 to 78.6) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

| End point title | Overall Survival (OS) |
|---|---|

End point description:

Overall survival was defined as the time interval from the date of first study treatment administration to death from any cause. It was estimated using the Kaplan-Meier method. Confidence interval (CI) for Kaplan-Meier estimates were calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley. The EP consisted of evaluable participants from the AT population who received at least 1 full dose of isatuximab in Cycle 1 and who had at least 1 valid response value that was evaluable. 99999 = Upper limit of CI was not estimable due to insufficient number of participants with events at study closure.

| End point type | Secondary |
|---|---|

End point timeframe:

From first study treatment administration up to death due to any cause, a maximum of 45 months

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 11 | 23 | |
| Units: months | | | | |
| median (confidence interval 95%) | 12.09 (3.975 to 99999) | 6.85 (2.201 to 99999) | 9.40 (5.947 to 99999) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Event-Free Survival (EFS)

| End point title | Event-Free Survival (EFS) |
|---|---|

End point description:

The EFS was defined as the time interval from the date of first study treatment administration to the date of the first of: completion or going off protocol induction/consolidation therapy without CR, relapse from CR, or death due to any cause, whichever occurred first. It was estimated using the Kaplan-Meier method. CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley. The EP consisted of evaluable participants from the AT population who received at least 1 full dose of isatuximab in Cycle 1 and who had at least 1 valid response value that was evaluable. 99999 = Upper limit of CI was not estimable due to insufficient number of participants with events at study closure.

| End point type | Secondary |
|---|---|

End point timeframe:

From study treatment administration up to the date of first documented disease progression or death due to any cause, a maximum of 45 months

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 11 | 23 | |
| Units: months | | | | |
| median (confidence interval 95%) | 2.23 (1.413 to 99999) | 2.14 (1.347 to 99999) | 5.65 (1.347 to 99999) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DoR)

| End point title | Duration of Response (DoR) |
|---|---|

End point description:

The DoR was defined as the time from the date of the first complete response to the event date of first disease progression or death from any cause, whichever happened first. It was estimated using the Kaplan-Meier method. CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley. The EP consisted of evaluable participants from the AT population who received at least 1 full dose of isatuximab in Cycle 1 and who had at least 1 valid response value that was evaluable. Only responders were included in this analysis. -99999= Lower limit of CI not estimable due to insufficient number of participants with events at study closure. 99999= Upper limit of CI was not estimable due to insufficient number of participants with events at study closure.

| End point type | Secondary |
|---|---|

End point timeframe:

From first documented response up to the date of first documented disease progression or death due to any cause, a maximum of 45 months

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 5 | 14 | |
| Units: months | | | | |
| median (confidence interval 95%) | 7.26 (-99999 to 99999) | 1.18 (0.887 to 99999) | 4.40 (-99999 to 99999) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cluster of Differentiation (CD)38 Receptor Density

| End point title | Cluster of Differentiation (CD)38 Receptor Density |
|---|---|

End point description:

Blood samples were collected to assess CD38 receptor density as a predictive biomarker. It was assessed across complete responders and non-complete responders. The Antibody Binding Capacity (ABC) was calculated using the following equation: ABC = 10^(Logarithm(Mean Fluorescence Intensity)*a+b) where "a" was the slope and "b" was the Y-intercept of the calibration curve equation. Specific and absolute quantitative values (specific antibody-binding capacity [sABC]) of binding of the selected antibodies were calculated after subtraction of the negative isotypic immunoglobulin G (IgG) control. The EP consisted of evaluable participants from the AT population who received at least 1 full dose of isatuximab in Cycle 1 and who had at least 1 valid response value that was evaluable. Only those participants with data available at specified timepoints were analyzed and denoted by 'n' in the categories . 99999 = SD cannot be derived for a single participant. NK=Natural killer cells.

| End point type | Secondary |
|---|---|

End point timeframe:

Pre-dose on Day 1

| End point values | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 11 | 23 | |
| Units: specific antibody-binding capacity | | | | |
| arithmetic mean (standard deviation) | | | | |
| Blood blast cells: CR/CRi (n=5,2,3) | 20345.6 (± 23439.7) | 12780.0 (± 15559.2) | 19502.0 (± 20919.7) | |
| Blood blast cells: Non CR/CRi (n=2,1,2) | 31080.0 (± 2397.1) | 22952.0 (± 99999) | 9815.0 (± 4203.0) | |
| Blood immune cells (NK cells): CR/CRi (n=5,2,3) | 13506.2 (± 3018.6) | 22639.0 (± 1796.1) | 11220.3 (± 3764.6) | |
| Blood immune cells (NK cells):Non CR/CRi (n=2,1,2) | 16650.0 (± 851.4) | 33859.0 (± 99999) | 22530.0 (± 685.9) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: CD38 Receptor Occupancy

| End point title | CD38 Receptor Occupancy |
|---|---|

End point description:

Blood samples were collected to assess CD38 receptor occupancy as a pharmacodynamics marker. It was assessed across complete responders and non-complete responders. Multicolor flow cytometry assay was validated for CD38 receptor occupancy (CD38RO) quantification, based on the use of 2 murine monoclonal antibodies (MAbs), one competing with SAR650984 to determine number of free CD38 receptors (MAb1) and one recognizing a different binding epitope on CD38 to measure total number of receptors (MAb2) at cell surface of the cancer cells. Cells were tagged with either MAb1 (Tube #1) or MAb2 (Tube #2). The percentage RO was calculated using following equation: % CD38RO = [(sABC MAb2 - sABC MAb1)/sABC MAb2] X 100. The EP consisted of evaluable participants from AT

population who received at least 1 full dose of isatuximab in Cycle 1 and who had at least 1 valid response value that was evaluable. Only those participants with data available at specified timepoints were analyzed; denoted by 'n'.

| End point type | Secondary |
|---|---|

End point timeframe:

Pre-dose on Day 15

| **End point values** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | T-cell Acute Lymphoblastic Leukemia (T-ALL) | Acute Myeloid Leukemia (AML) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 11 | 23 | |
| Units: percent receptor occupancy | | | | |
| arithmetic mean (standard deviation) | | | | |
| Blood plasma cells: CR/CRi (n=0,2,0) | 9999 (± 9999) | 40.5 (± 30.4) | 9999 (± 9999) | |
| Blood plasma cells: Non CR/CRi (n=1,1,0) | 44.0 (± 99999) | 55.0 (± 99999) | 9999 (± 9999) | |
| Blood NK cells: CR/CRi (n=5,3,0) | 55.6 (± 6.9) | 66.7 (± 2.1) | 9999 (± 9999) | |
| Blood NK cells: Non CR/CRi (n=3,1,0) | 61.3 (± 3.5) | 70.0 (± 99999) | 9999 (± 9999) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the time of the first treatment administration (Day 1) up to 30 days after the last treatment (maximum duration of exposure of 13.1 weeks for B-ALL cohort, 10.7 weeks for T-ALL cohort and 7.1 weeks for AML cohort)

Adverse event reporting additional description:

Analysis was performed on the AT population.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 26.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | B-cell Acute Lymphoblastic Leukemia (B-ALL) |

Reporting group description:

Participants with B-ALL received isatuximab 20 mg/kg IV infusion QW for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and Q2W during the consolidation period (i.e., on Days 29, 43, and 57. Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| | |
|---|---|
| Reporting group title | All Participants |

Reporting group description:

All participants in the study were included in this cohort.

| | |
|---|---|
| Reporting group title | Acute Myeloid Leukemia (AML) |

Reporting group description:

Participants with AML received isatuximab 20 mg/kg IV infusion on Days 1, 8, and 15 of each Cycle (up to 2 treatment cycles, each cycle 28 days). Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| | |
|---|---|
| Reporting group title | T-cell Acute Lymphoblastic Leukemia (T-ALL) |

Reporting group description:

Participants with T-ALL received isatuximab 20 mg/kg IV infusion QW for 4 weeks during the induction period (i.e., on Days 1, 8, 15, and 22) and Q2W during the consolidation period (i.e., on Days 29, 43, and 57. Participants received recommended isatuximab premedication as per protocol. Starting on Day 8, combination chemotherapies were added. Participants without documented disease progression at EOT visit who had not started treatment with another anticancer therapy received follow-up visits every 2 months until initiation of another anticancer therapy, disease progression, death, or final analysis cut-off date, whichever occurred first. Participants with documented disease progression/initiation of new anticancer treatment were followed for survival every 4 months until death or final analysis cut-off date, whichever occurred first.

| **Serious adverse events** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | All Participants | Acute Myeloid Leukemia (AML) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 27 (70.37%) | 48 / 67 (71.64%) | 17 / 27 (62.96%) |
| number of deaths (all causes) | 17 | 43 | 18 |
| number of deaths resulting from adverse events | 3 | 5 | 2 |
| Injury, poisoning and procedural complications | | | |
| Infusion Related Reaction | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic Aneurysm | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac Failure | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised Tonic-Clonic Seizure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Febrile Bone Marrow Aplasia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile Neutropenia | | | |
| subjects affected / exposed | 10 / 27 (37.04%) | 22 / 67 (32.84%) | 7 / 27 (25.93%) |
| occurrences causally related to treatment / all | 11 / 12 | 26 / 29 | 9 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 4 / 67 (5.97%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Haemophagocytic Lymphohistiocytosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic Shock | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytokine Release Syndrome | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Gastrointestinal disorders | | | |
| Neutropenic Colitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis Acute | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mouth Haemorrhage | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal Fissure | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| Epistaxis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatic Failure | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Bone Pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated Aspergillosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device Related Infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Catheter Site Infection | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial Sepsis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia Sepsis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Genital Herpes Zoster | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fungal Sepsis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Fungal Infection | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fournier's Gangrene | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Neutropenic Sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis Externa | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal Bacteraemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis Fungal | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic Shock | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | 8 / 67 (11.94%) | 3 / 27 (11.11%) |
| occurrences causally related to treatment / all | 2 / 3 | 6 / 8 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 4 / 67 (5.97%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Rhinovirus Infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonal Sepsis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 2 / 27 (7.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis Jirovecii Pneumonia | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal Infection | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | T-cell Acute Lymphoblastic Leukemia (T-ALL) | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 13 (92.31%) | | |
| number of deaths (all causes) | 8 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Infusion Related Reaction | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Aortic Aneurysm | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac Failure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Generalised Tonic-Clonic Seizure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile Bone Marrow Aplasia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile Neutropenia | | | |
| subjects affected / exposed | 5 / 13 (38.46%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Neutropenia | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancytopenia | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune system disorders | | | | |
| Haemophagocytic Lymphohistiocytosis | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anaphylactic Shock | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cytokine Release Syndrome | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Neutropenic Colitis | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis Acute | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mouth Haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal Fissure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatic Failure | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Bone Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Encephalitis | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disseminated Aspergillosis | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device Related Infection | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Catheter Site Infection | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacterial Sepsis | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia Sepsis | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Genital Herpes Zoster | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal Sepsis | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal Infection | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fournier's Gangrene | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutropenic Sepsis | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Otitis Externa | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal Bacteraemia | | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis Fungal | | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic Shock | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rhinovirus Infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pseudomonal Sepsis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumocystis Jirovecii Pneumonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal Infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | B-cell Acute Lymphoblastic Leukemia (B-ALL) | All Participants | Acute Myeloid Leukemia (AML) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 26 / 27 (96.30%) | 62 / 67 (92.54%) | 24 / 27 (88.89%) |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 1 / 27 (3.70%) |
| occurrences (all) | 1 | 3 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 8 / 67 (11.94%) | 3 / 27 (11.11%) |
| occurrences (all) | 0 | 10 | 3 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 3 | 2 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 10 / 27 (37.04%) | 26 / 67 (38.81%) | 12 / 27 (44.44%) |
| occurrences (all) | 14 | 43 | 23 |
| Oedema Peripheral | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 6 / 67 (8.96%) | 3 / 27 (11.11%) |
| occurrences (all) | 2 | 8 | 5 |
| Face Oedema | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 3 / 67 (4.48%) | 0 / 27 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences (all) | 0 | 2 | 1 |
| Catheter Site Pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences (all) | 0 | 3 | 2 |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Food Allergy | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 3 / 67 (4.48%) | 3 / 27 (11.11%) |
| occurrences (all) | 0 | 5 | 5 |
| Cough | | | |
| subjects affected / exposed | 6 / 27 (22.22%) | 8 / 67 (11.94%) | 1 / 27 (3.70%) |
| occurrences (all) | 8 | 10 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 5 / 67 (7.46%) | 2 / 27 (7.41%) |
| occurrences (all) | 2 | 5 | 2 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 3 | 3 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 4 / 67 (5.97%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 4 | 2 |
| Irritability | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Insomnia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences (all) | 0 | 2 | 1 |
| Investigations | | | |
| Weight Decreased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 4 / 67 (5.97%) | 1 / 27 (3.70%) |
| occurrences (all) | 2 | 4 | 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infusion Related Reaction | | | |
| subjects affected / exposed | 8 / 27 (29.63%) | 26 / 67 (38.81%) | 14 / 27 (51.85%) |
| occurrences (all) | 12 | 33 | 16 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 5 / 67 (7.46%) | 2 / 27 (7.41%) |
| occurrences (all) | 2 | 5 | 2 |
| Nervous system disorders | | | |
| Dysaesthesia | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Facial Paralysis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | 15 / 67 (22.39%) | 9 / 27 (33.33%) |
| occurrences (all) | 3 | 21 | 14 |
| Peripheral Sensory Neuropathy | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Tremor | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 4 / 67 (5.97%) | 1 / 27 (3.70%) |
| occurrences (all) | 2 | 5 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 1 / 27 (3.70%) |
| occurrences (all) | 1 | 3 | 1 |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Febrile Neutropenia | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | 10 / 67 (14.93%) | 5 / 27 (18.52%) |
| occurrences (all) | 6 | 12 | 5 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 6 | 5 |
| Eye disorders | | | |
| Eyelid Oedema | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Periorbital Oedema | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 6 / 27 (22.22%) | 12 / 67 (17.91%) | 5 / 27 (18.52%) |
| occurrences (all) | 6 | 17 | 8 |
| Anal Fissure | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | 5 / 67 (7.46%) | 2 / 27 (7.41%) |
| occurrences (all) | 5 | 7 | 2 |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 4 / 67 (5.97%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 4 | 2 |
| Anal Inflammation | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 0 / 27 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Constipation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 27 (11.11%) | 12 / 67 (17.91%) | 7 / 27 (25.93%) |
| occurrences (all) | 3 | 13 | 7 |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | 15 / 67 (22.39%) | 8 / 27 (29.63%) |
| occurrences (all) | 5 | 17 | 9 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 5 / 67 (7.46%) | 4 / 27 (14.81%) |
| occurrences (all) | 0 | 7 | 6 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences (all) | 0 | 3 | 2 |
| Nausea | | | |
| subjects affected / exposed | 9 / 27 (33.33%) | 18 / 67 (26.87%) | 6 / 27 (22.22%) |
| occurrences (all) | 17 | 31 | 9 |
| Oral Pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 1 / 27 (3.70%) |
| occurrences (all) | 0 | 2 | 1 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 10 / 27 (37.04%) | 22 / 67 (32.84%) | 8 / 27 (29.63%) |
| occurrences (all) | 10 | 23 | 8 |
| Vomiting | | | |
| subjects affected / exposed | 6 / 27 (22.22%) | 19 / 67 (28.36%) | 10 / 27 (37.04%) |
| occurrences (all) | 7 | 25 | 15 |
| Colitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 5 / 67 (7.46%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 5 | 2 |
| Hepatobiliary disorders | | | |
| Hepatic Steatosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hepatic Failure | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| Dry Skin | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Alopecia | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 3 / 67 (4.48%) | 0 / 27 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 4 | 3 |
| Rash | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 6 / 67 (8.96%) | 6 / 27 (22.22%) |
| occurrences (all) | 0 | 7 | 7 |
| Rash Maculo-Papular | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 3 / 67 (4.48%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 7 | 6 |
| Renal and urinary disorders | | | |
| Nephropathy Toxic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal Tubular Necrosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary Retention | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 6 / 67 (8.96%) | 1 / 27 (3.70%) |
| occurrences (all) | 2 | 7 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 4 / 67 (5.97%) | 3 / 27 (11.11%) |
| occurrences (all) | 0 | 4 | 3 |
| Bone Pain | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 3 / 67 (4.48%) | 1 / 27 (3.70%) |
| occurrences (all) | 2 | 3 | 1 |
| Neck Pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 3 / 67 (4.48%) | 3 / 27 (11.11%) |
| occurrences (all) | 0 | 3 | 3 |

| | | | |
|---|---|---|---|
| Pain In Extremity | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | 8 / 67 (11.94%) | 2 / 27 (7.41%) |
| occurrences (all) | 6 | 13 | 5 |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 4 / 67 (5.97%) | 2 / 27 (7.41%) |
| occurrences (all) | 1 | 4 | 2 |
| Device Related Infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 3 / 67 (4.48%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 3 | 2 |
| Lip Infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral Candidiasis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral Herpes | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Respiratory Syncytial Virus Infection | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 2 / 67 (2.99%) | 0 / 27 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Skin Infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 2 / 67 (2.99%) | 2 / 27 (7.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Viral Rhinitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 11 / 67 (16.42%) | 8 / 27 (29.63%) |
| occurrences (all) | 1 | 11 | 8 |
| Increased Appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 67 (1.49%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| **Non-serious adverse events** | T-cell Acute Lymphoblastic Leukemia (T-ALL) | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 13 (92.31%) | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 5 / 13 (38.46%) | | |
| occurrences (all) | 7 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | | |
| occurrences (all) | 6 | | |
| Oedema Peripheral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Face Oedema | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Chills | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Catheter Site Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Food Allergy | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cough | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Irritability | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 13 (7.69%)<br>1 | | |
| Investigations<br>Weight Decreased<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 13 (7.69%)<br>1 | | |
| Injury, poisoning and procedural complications<br>Contusion<br>subjects affected / exposed<br>occurrences (all)<br><br>Infusion Related Reaction<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 13 (7.69%)<br>1<br><br><br>4 / 13 (30.77%)<br>5 | | |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 13 (7.69%)<br>1 | | |
| Nervous system disorders<br>Dysaesthesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Dysgeusia<br>subjects affected / exposed<br>occurrences (all)<br><br>Facial Paralysis<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Peripheral Sensory Neuropathy<br>subjects affected / exposed<br>occurrences (all)<br><br>Seizure<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 13 (7.69%)<br>1<br><br><br>0 / 13 (0.00%)<br>0<br><br><br>1 / 13 (7.69%)<br>1<br><br><br>3 / 13 (23.08%)<br>4<br><br><br>1 / 13 (7.69%)<br>1<br><br><br>1 / 13 (7.69%)<br>1 | | |

| | | | |
|---|---|---|---|
| Tremor | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 2 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Febrile Neutropenia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Eyelid Oedema | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 2 | | |
| Periorbital Oedema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 3 | | |
| Anal Fissure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Anal Inflammation | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences (all) | 3 | | |
| Constipation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences (all) | 3 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | | |
| occurrences (all) | 3 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | | |
| occurrences (all) | 5 | | |
| Oral Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | | |
| occurrences (all) | 5 | | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | | |
| occurrences (all) | 3 | | |
| Colitis | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences (all) | 2 | | |
| Hepatobiliary disorders | | | |
| Hepatic Steatosis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Hepatic Failure | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| Dry Skin | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash Maculo-Papular | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Nephropathy Toxic | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Renal Tubular Necrosis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Urinary Retention | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | | |
| occurrences (all) | 4 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Bone Pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neck Pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---|---|---|
| Pain In Extremity | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Device Related Infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Lip Infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Oral Candidiasis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Oral Herpes | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Respiratory Syncytial Virus Infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin Infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral Rhinitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences (all) | 2 | | |
| Increased Appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 13 (7.69%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 March 2019 | Clarified the suspected unexpected serious adverse reactions and sponsor responsibilities to submit any change(s) considered substantial to the regulatory authorities for notification and approval. Clarified the contraception and pregnancy testing for females and males of childbearing potential, as well as the criteria for discontinuation of the study by the Sponsor. Updated the PK follow-up assessment from 60 to 90 days after last isatuximab administration to align with other isatuximab studies. Improved the feasibility of the study procedures. Clarified that administrative and editorial updates and corrections to the protocol will be performed. |
| 04 December 2019 | Clarified the definition of CR, in order to avoid participants being 'not evaluable' if still dependent on red blood cell transfusions. Included dexamethasone as an intervention for ALL cohort as part of study treatment. Further clarified the difference that for AML cohort dexamethasone is optional, except as premedication for isatuximab. Updated the duration for contraception. Added Montelukast as a systematic premedication, the objective being to decrease the incidence and severity of IRs; it should not be at Investigator's discretion. Added hematological criteria for ALL participants before starting the consolidation period. Simplified some procedures in order to be closer to clinical practice. Added recommendations in case of pegaspargase hypersensitivity. Added analysis of CD38 receptor density and occupancy, in order to better understand the response profile at the end of the trial. Clarified on the first interim analysis that was to be performed on first 20 participants. Clarified that administrative and editorial updates and corrections to the protocol will be performed. |
| 30 July 2020 | Protocol was amended to implement changes following health Authorities comments and to mitigate the risk of hepatitis reactivation identified in the SAR650984 Investigator's Brochure edition 11 (30-Apr-2020). |
| 24 November 2020 | Implemented data monitoring committee (DMC) recommendations following the occurrence of first fatal case as an outcome of a Cytokine Release Syndrome (CRS) event. On 01 October 2020, due to the occurrence of first fatal CRS event, the study DMC had evaluated the safety profile of the first 9 treated participants and recommended the continuation of the study with changes to be implemented in an amendment to the protocol. The main changes were: White blood cell (WBC) counts to be below 20 x 10^9/L before isatuximab administration. Participants with high WBC counts between 20 and 50 x 10^9/L at screening and with high tumor burden in relation to extramedullary disease should receive a rescue cytoreductive therapy with a short half-life in order to potentially reach the 20 x 10^9/L WBC threshold before first isatuximab administration. As consequence, the list of cytoreductive drugs with suggested doses were proposed in this amendment in order to have less heterogeneity in the participants' cytoreductive therapy management across participating sites. Guidance was added to clarify the CRS events with inclusion of a specific section and table describing criteria for diagnosis, grading, as well as management of these events. Prospective determinations of CRS biomarkers at different time points were included. Cytokines panel, ferritin, and C-reactive protein (CRP) were added at baseline and at different time points in order to better assess events like CRS, hemophagocytic lymphohistiocytosis (HLH), infections, etc. Moreover, specific guidance for hematology, vital signs, radiology were added in case of high tumor burden or CRS events. Anti-interleukin 6 as concomitant or rescue medication in case of CRS Grade 2 or above was added. Clarified that seizures >=Grade 3 should be reported as adverse events of special interest (AESI). |

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|---|---|
| 14 October 2021 | Protocol was amended to allow the enrollment of children <2 years old as after PK assessment, the dose of 20 mg/kg was confirmed in this young subpopulation. The main changes were: Justification of the dose (20 mg/kg) for children <2 years old. Definition of evaluable participant update. Clarification on coagulation test frequency. Added the possibility to perform a positron emission tomography (PET)-magnetic resonance imaging instead of PET-computed tomography when |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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| The study was prematurely stopped due to sponsor decision (stage 2 efficacy criteria not met) and not due to safety concerns. |

Notes: