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	v2 (current)
This version publication date	29 June 2024
First version publication date	02 December 2023
Version creation reason	• Changes to summary attachments Results summary aligned with ClinicalTrials.gov

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 Units: Subjects			
Age continuous Units: years			
arithmetic mean	8.22	8.72	9.04
standard deviation	± 3.92	± 4.15	± 5.41
Gender categorical Units: Subjects			
Female	10	4	12
Male	17	9	15
Race 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. 22222= 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 (± 22222)		
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:

MRD assessment was performed centrally 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 was analyzed. In AML indication, peripheral blood tissue is not representative of the tumor burden and cannot be used to assess MRD. 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=No evaluable participants.

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, 10^-6 (n=13, 5, 0)	3	1	9999	
Bone marrow, 10^-6 (n=13, 5, 14)	0	2	0	
Bone marrow, 10^-3 (n=0, 0, 14)	9999	9999	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 . 22222= 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 (± 22222)	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 (± 22222)	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. Analysis was performed on the EP. Only those

participants with data available at specified timepoints were analyzed; denoted by 'n'. 22222=SD cannot be derived for a single participant. 9999=No evaluable participants.

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 (± 22222)	55.0 (± 22222)	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 (± 22222)	9999 (± 9999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs=from time of 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). Deaths=a maximum of 45 months

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

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.

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

Notes: