Clinical trial results:
A Phase 4, Open-Label, Randomized Study of two Inotuzumab Ozogamicin Dose Levels In Adult Participants With Relapsed Or Refractory B-Cell Acute Lymphoblastic Leukemia Eligible for Hematopoietic Stem Cell Transplantation and who Have Risk Factor(S) for Veno-Occlusive Disease

Summary

EudraCT number	2018-001557-27
Trial protocol	PL BE HU ES
Global end of trial date	26 May 2023

Results information

Result version number	v1 (current)
This version publication date	08 June 2024
First version publication date	08 June 2024

Trial information

Trial identification

Sponsor protocol code	B1931030

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03677596
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	27 November 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 rates of veno-occlusive disease (VOD) and hematologic remission (complete remission/complete remission with incomplete hematologic recovery [CR/Cri]) for 2 Inotuzumab Ozogamicin dose levels in adult subjects with relapsed or refractory B-cell Acute lymphocytic leukemia (ALL) who are eligible for hematopoietic stem cell transplant (HSCT) and who are at higher risk for developing VOD post-HSCT.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	India: 14
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Singapore: 5
Country: Number of subjects enrolled	Türkiye: 43
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	102
EEA total number of subjects	31

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	95
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 102 were enrolled and treated. In Run-in Phase, 22 subjects were enrolled and treated. In Randomised Phase, 80 subjects were enrolled and treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)

Arm description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete remission (CR)/complete remission with incomplete hematologic recovery (CRi) is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15). The maximum treatment duration was approximately 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Inotuzumab Ozogamicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

1.2 mg/m²/cycle administered in 3 divided doses (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously.

Arm title	1.8 mg/m²/cycle (Dose Level 1 Randomized Phase)

Arm description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle administrated in 3 divided doses (0.8 mg/m² on Day 1, 0.5 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Inotuzumab Ozogamicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

1.8 mg/m²/cycle administrated in 3 divided doses (0.8 mg/m² on Day 1, 0.5 mg/m² on Days 8 and 15) intravenously.

Number of subjects in period 1	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.8 mg/m²/cycle (Dose Level 1 Randomized Phase)
Started	64	38
Completed	41	19
Not completed	23	19
Adverse event, serious fatal	10	6
Consent withdrawn by subject	3	-
Disease Relapse	2	2
Adverse event, non-fatal	-	1
Progressive Disease	8	8
Unspecified	-	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)
Reporting group description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete remission (CR)/complete remission with incomplete hematologic recovery (CRi) is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15). The maximum treatment duration was approximately 26 weeks.	
Reporting group title	1.8 mg/m²/cycle (Dose Level 1 Randomized Phase)
Reporting group description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle administrated in 3 divided doses (0.8 mg/m² on Day 1, 0.5 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	

Reporting group values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.8 mg/m²/cycle (Dose Level 1 Randomized Phase)	Total
Number of subjects	64	38	102
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	59	36	95
>=65 years	5	2	7
Age continuous Units: years			
arithmetic mean	43.27	39.47	
standard deviation	± 14.85	± 15.26	-
Sex: Female, Male Units: Subjects			
Female	28	18	46
Male	36	20	56
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	11	11	22
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	51	25	76
More than one race	0	0	0
Unknown or Not Reported	2	2	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	3	10
Not Hispanic or Latino	56	35	91
Unknown or Not Reported	1	0	1
ECOG Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light			

house work, office work; ECOG=2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			
ECOG = 0	28	20	48
ECOG = 1	33	13	46
ECOG = 2	3	5	8
Body Mass Index (BMI)			
BMI (kg/m^2) was computed as Height (cm)/Weight (kg) x 100.			
Units: kg/m^2			
median	25.26	24.78	
full range (min-max)	16 to 39	16 to 41	-
Body Surface Area (BSA)			
BSA (m^2) will be computed using Du Bois Formula: 0.007184 x Weight (kg)^0.425 x Height (cm)^0.725.			
Units: m^2			
median	1.84	1.79	
full range (min-max)	1 to 3	1 to 3	-

Subject analysis sets

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomized)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomized)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Reporting group values	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Number of subjects	22	42	42
Age Categorical Units: Subjects			
<=18 years Between 18 and 65 years >=65 years			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
ECOG Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			
ECOG = 0			

ECOG = 1			
ECOG = 2			

Body Mass Index (BMI)			
BMI (kg/m^2) was computed as Height (cm)/Weight (kg) x 100.			
Units: kg/m^2			
median			
full range (min-max)			
Body Surface Area (BSA)			
BSA (m^2) will be computed using Du Bois Formula: 0.007184 x Weight (kg)^0.425 x Height (cm)^0.725.			
Units: m^2			
median			
full range (min-max)			

Reporting group values	1.8 mg/m²/cycle (Dose Level 1 Randomised)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Number of subjects	38	10	21
Age Categorical			
Units: Subjects			
<=18 years			
Between 18 and 65 years			
>=65 years			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			
ECOG Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			

ECOG = 0 ECOG = 1 ECOG = 2			
Body Mass Index (BMI)			
BMI (kg/m^2) was computed as Height (cm)/Weight (kg) x 100.			
Units: kg/m^2 median full range (min-max)			
Body Surface Area (BSA)			
BSA (m^2) will be computed using Du Bois Formula: 0.007184 x Weight (kg)^0.425 x Height (cm)^0.725.			
Units: m^2 median full range (min-max)			

Reporting group values	1.8 mg/m²/cycle (Dose Level 1 Randomised)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Number of subjects	12	22	11
Age Categorical Units: Subjects			
<=18 years Between 18 and 65 years >=65 years			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
ECOG Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			

ECOG = 0 ECOG = 1 ECOG = 2			
Body Mass Index (BMI)			
BMI (kg/m^2) was computed as Height (cm)/Weight (kg) x 100.			
Units: kg/m^2 median full range (min-max)			
Body Surface Area (BSA)			
BSA (m^2) will be computed using Du Bois Formula: 0.007184 x Weight (kg)^0.425 x Height (cm)^0.725.			
Units: m^2 median full range (min-max)			

Reporting group values	1.2 mg/m²/cycle (Dose Level 2 Randomized)	1.8 mg/m²/cycle (Dose Level 1 Randomised)	1.2 mg/m²/cycle (Dose Level 2 Randomized)
Number of subjects	35	26	41
Age Categorical Units: Subjects			
<=18 years Between 18 and 65 years >=65 years			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
ECOG Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			

ECOG = 0 ECOG = 1 ECOG = 2			
Body Mass Index (BMI)			
BMI (kg/m^2) was computed as Height (cm)/Weight (kg) x 100.			
Units: kg/m^2 median full range (min-max)			
Body Surface Area (BSA)			
BSA (m^2) will be computed using Du Bois Formula: 0.007184 x Weight (kg)^0.425 x Height (cm)^0.725.			
Units: m^2 median full range (min-max)		18	

Reporting group values	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Number of subjects	2	3	3
Age Categorical Units: Subjects			
<=18 years Between 18 and 65 years >=65 years			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
ECOG Performance Status			
Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			

ECOG = 0 ECOG = 1 ECOG = 2			
Body Mass Index (BMI)			
BMI (kg/m^2) was computed as Height (cm)/Weight (kg) x 100.			
Units: kg/m^2 median full range (min-max)			
Body Surface Area (BSA)			
BSA (m^2) will be computed using Du Bois Formula: 0.007184 x Weight (kg)^0.425 x Height (cm)^0.725.			
Units: m^2 median full range (min-max)			

End points reporting groups

Reporting group title	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)
Reporting group description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete remission (CR)/complete remission with incomplete hematologic recovery (CRi) is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15). The maximum treatment duration was approximately 26 weeks.	
Reporting group title	1.8 mg/m²/cycle (Dose Level 1 Randomized Phase)
Reporting group description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle administrated in 3 divided doses (0.8 mg/m² on Day 1, 0.5 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	
Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	
Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	
Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	
Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	
Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.	
Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The	

maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomized)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomized)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Run-in)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle (0.6 mg/m² on Day 1, 0.3 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The

maximum treatment duration was approximately 26 weeks.

Subject analysis set title	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

Primary: Percentage of Subjects With Veno-occlusive Disease (VOD)

End point title	Percentage of Subjects With Veno-occlusive Disease (VOD)[1][2]

End point description:

VOD happened when the small blood vessels that lead into the liver and were inside the liver become blocked. VOD is defined as: a. Classical VOD (first 21 days after HSCT): Bilirubin>=2 mg/dL and 2 (or more) of the following criteria must also be present: 1. Painful hepatomegaly; 2. Weight gain >5%; 3. Ascites. b. Late onset VOD (>21 days after HSCT): Classical VOD beyond Day 21; or Histologically proven VOD; or Two or more of the following criteria must be present: 1. Bilirubin >2 mg/dL; 2. Painful hepatomegaly; 3. Weight gain >5%; 4. Ascites. and hemodynamical and/or ultrasound evidence of VOD. All randomised subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

From consent up to follow-up (up to 2 years)

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: No statistical analysis was planned for this endpoint

[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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Percentage of subjects				
number (not applicable)	12.5	9.1	14.3	5.3

Statistical analyses

No statistical analyses for this end point

Primary: Rate of Hematologic Remission (Complete Response [CR] / Complete Response with Incomplete Hematologic Recovery[CRi])

End point title	Rate of Hematologic Remission (Complete Response [CR] / Complete Response with Incomplete Hematologic Recovery[CRi])[3][4]

End point description:

CR=disappearance of leukemia indicated by <5% marrow blasts, absence of peripheral blood leukemic blasts,recovery of hematopoiesis defined by absolute neutrophil count (ANC)>=1000/µL and platelets>=100000/µL. C1 extramedullary disease status is required. CRi = CR except with ANC <1000/µL and/or platelets <100000/µL. Subjects randomised into study with study drug assignment based on randomisation.

End point type	Primary

End point timeframe:

From first dose of study treatment till follow-up of up to 2 years

Notes:

[3] - 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: No statistical analysis was planned for this endpoint

[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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Percentage of subjects				
number (not applicable)	71.9	50.0	83.3	68.4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (Treatment-related)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (Treatment-related)[5]

End point description:

Adverse event (AE) = any untoward medical occurrence in subject who received study treatment without regard to possibility of causal relationship. Treatment emergent AEs (TEAEs) were defined as AEs that reported the period starting with the first dose of study treatment drug through 63 days after last dose or 1 day before start day of new anticancer therapy, whichever occurred first. A SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Grades of severity were defined by CTCAE v3.0. Grade 3 = severe adverse event; Grade 4 = life-threatening consequences; urgent intervention indicated. Grade 5 = death related to AE. Causality of TEAEs were assessed by the Investigator. All randomised subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Subjects				

Participants with AEs	31	13	18	22
Participants with SAEs	15	7	8	10
Participants with Maximum Grade 3 or 4 AEs	20	9	11	11
Participants with Maximum Grade 5 AEs	2	1	1	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (All Causalities)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (All Causalities)[6]

End point description:

Adverse event (AE) = any untoward medical occurrence in subject who received study treatment without regard to possibility of causal relationship. On-treatment period was defined as the period starting with the 1st dose of study treatment through 63 days after last dose or 1 day before start day of new anticancer therapy, whichever occurred first. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. All VOD cases were reported as SAE. Grades of severity were defined by Common terminology criteria for adverse events (CTCAE) v3.0. Grade 3=severe adverse event; Grade 4=life-threatening consequences; urgent intervention indicated. Grade 5=death related to AE. All randomised subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Subjects				
Subjects with AE	60	21	39	35
Subjects with SAEs	43	15	28	21
Subjects with Maximum Grade 3 or 4 AE	30	9	21	18
Subjects with Maximum Grade 5 adverse events	19	7	12	10

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Serious Adverse Events

(Post-HSCT)

End point title	Number of Subjects With Treatment-Emergent Serious Adverse Events (Post-HSCT)[7]

End point description:

A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. All SAEs occurred after HSCT were reported in this endpoint. All randomised subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Starting from the first transplant after inotuzumab ozogamicin treatment and including the entire duration of subsequent follow up (approximately 52 weeks)

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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Subjects	14	6	8	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Shift Summary of Hematology Laboratory Test Results from Grade Less Than or Equal to (<=) 2 at Baseline to Grade 3 or 4 Post-Baseline

End point title	Number of Subjects With Shift Summary of Hematology Laboratory Test Results from Grade Less Than or Equal to (<=) 2 at Baseline to Grade 3 or 4 Post-Baseline[8]

End point description:

Baseline assessment was defined as the last assessment performed on or prior to the date of the first dose of study treatment. Following Parameters were analyzed for laboratory assessment: Hematology (Activated partial thromboplastin time prolonged, Anemia, Hemoglobin increased, International normalization rate (INR) increased, Leukocytosis, Lymphocyte count decreased, Lymphocyte count increased, Neutrophil count decreased, Platelet count decreased, White blood cell decreased). Grades of severity were defined by CTCAE v3.0. Grade 2 = moderate adverse event; Grade 3= severe adverse event; Grade 4 = life-threatening consequences; urgent intervention indicated. All randomised subjects who received at least 1 dose of study drug and with at least 1 postbaseline assessment in each treatment group. 'Number analysed' = subjects evaluable for this endpoint for each specified row. '99999'=Grade4 was not applicable for the test.

End point type	Secondary

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

Notes:

[8] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Subjects				
APT time prolonged - Grade 3 (n=51,19,32,27)	0	0	0	0
APT time prolonged - Grade 4 (n=51,19,32,27)	99999	99999	99999	99999
Anemia - Grade 3 (n=37,15,22,20)	21	8	13	11
Anemia - Grade 4 (n=37,15,22,20)	99999	99999	99999	99999
Hemoglobin increased - Grade 3(n=18,6,12,13)	0	0	0	0
Hemoglobin increased - Grade 4(n=18,6,12,13)	99999	99999	99999	99999
INR increased - Grade 3(n=27,11,16,12)	0	0	0	0
INR increased - Grade 4(n=27,11,16,12)	99999	99999	99999	99999
Leukocytosis - Grade 3(n=18,7,11,13)	1	1	0	0
Leukocytosis - Grade 4(n=18,7,11,13)	99999	99999	99999	99999
Lymphocyte count decreased-Grade 3(n=51,16,35,28)	16	1	15	7
Lymphocyte count decreased-Grade 4(n=51,16,35,28)	6	4	2	4
Lymphocyte count increased-Grade 3(n=27,13,14,17)	3	2	1	3
Lymphocyte count increased-Grade 4(n=27,13,14,17)	99999	99999	99999	99999
Neutrophil count decreased-Grade 3(n=51,17,34,27)	8	2	6	7
Neutrophil count decreased-Grade 4(n=51,17,34,27)	21	11	10	9
Platelet count decreased-Grade 3(n=41,13,28,28)	7	1	6	5
Platelet count decreased - Grade 4(n=41,13,28,28)	7	4	3	7
White blood cell decreased-Grade 3(n=56,18,38,29)	18	5	13	9
White blood cell decreased-Grade 4(n=56,18,38,29)	17	7	10	11

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Shift Summary of Chemistry Laboratory Test Results from Grade <=2 at Baseline to Grade 3 or 4 Post-Baseline

End point title	Number of Subjects With Shift Summary of Chemistry Laboratory Test Results from Grade <=2 at Baseline to Grade 3 or 4 Post-Baseline[9]

End point description:

Baseline assessment=last assessment performed on or prior to date of first dose of study treatment. Parameters analysed for laboratory assessment:Chemistry(Alanine aminotransferase[ALT] increased,

Alkaline phosphatase[ALP] increased,Aspartate aminotransferase[AST] increased,Blood bilirubin increased,Chronic kidney disease,Creatinine increased,Gamma glutamyl transpeptidase[GGT] increased,Hypercalcemia,Hyperglycemia,Hyperkalemia, Hypermagnesemia,Hypernatremia,Hypoalbuminemia,Hypocalcemia,Hypoglycemia,Hypokalemia,Hypomagnesemia, Hyponatremia,Hypophosphatemia,Lipase increased,Serum amylase increased).Grades of severity defined by CTCAE v3.0.Grade 2=moderate AE ;Grade 3=severe AE ;Grade 4= life-threatening consequences; urgent intervention indicated. All randomised subjects who received at least 1 dose of study drug with at least 1 postbaseline assessment in each treatment group.'Number analysed'= subjects evaluable for each specified row.'99999'=Grade4 was not applicable for the test.

End point type	Secondary

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

Notes:

[9] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Subjects				
ALT increased - Grade 3 (n=29,14,15,23)	1	1	0	0
ALT increased - Grade 4(n=29,14,15,23)	0	0	0	0
ALP increased - Grade 3 (n=42,14,28,22)	1	1	0	1
ALP increased - Grade 4 (n=42,14,28,22)	0	0	0	0
AST increased - Grade 3(n=42,16,26,26)	4	1	3	0
AST increased - Grade 4(n=42,16,26,26)	0	0	0	0
Blood bilirubin increased - Grade 3(n=31,14,17,20)	2	1	1	0
Blood bilirubin increased - Grade 4(n=31,14,17,20)	0	0	0	0
Chronic kidney disease - Grade 3(n=9,2,7,7)	0	0	0	0
Chronic kidney disease - Grade 4(n=9,2,7,7)	0	0	0	0
Creatinine increased - Grade 3(n=50,19,31,26)	0	0	0	0
Creatinine increased - Grade 4(n=50,19,31,26)	0	0	0	0
GGT increased - Grade 3(n=37,15,22,26)	3	1	2	3
GGT increased - Grade 4(n=37,15,22,26)	0	0	0	0
Hypercalcemia - Grade 3(n=22,10,12,15)	0	0	0	0
Hypercalcemia - Grade 4(n=22,10,12,15)	0	0	0	0
Hyperglycemia - Grade 3(n=37,13,24,21)	4	2	2	2
Hyperglycemia - Grade 4(n=37,13,24,21)	0	0	0	0

Hyperkalemia - Grade 3(n=21,10,11,14)	0	0	0	0
Hyperkalemia - Grade 4(n=21,10,11,14)	1	1	0	0
Hypermagnesemia - Grade 3(n=21,11,10,15)	1	1	0	1
Hypermagnesemia - Grade 4(n=21,11,10,15)	0	0	0	0
Hypernatremia - Grade 3(n=19,9,10,15)	0	0	0	0
Hypernatremia - Grade 4(n=19,9,10,15)	1	0	1	0
Hypoalbuminemia - Grade 3 (n=31,16,15,21)	4	1	3	3
Hypoalbuminemia - Grade 4(n=31,16,15,21)	99999	99999	99999	99999
Hypocalcemia - Grade 3(n=28,12,16,15)	1	1	0	0
Hypocalcemia - Grade 4(n=28,12,16,15)	0	0	0	0
Hypoglycemia - Grade 3(n=22,10,12,16)	0	0	0	0
Hypoglycemia - Grade 4(n=22,10,12,16)	0	0	0	0
Hypokalemia - Grade 3(n=32,13,19,24)	3	1	2	1
Hypokalemia - Grade 4(n=32,13,19,24)	1	1	0	0
Hypomagnesemia - Grade 3(n=30,14,16,18)	1	1	0	1
Hypomagnesemia - Grade 4(n=30,14,16,18)	0	0	0	1
Hyponatremia - Grade 3(n=27,13,14,19)	1	1	0	0
Hyponatremia - Grade 4(n=27,13,14,19)	0	0	0	0
Hypophosphatemia- Grade 3(n=26,13,13,18)	2	2	0	1
Hypophosphatemia - Grade 4(n=26,13,13,18)	0	0	0	1
Lipase increased - Grade 3(n=38,15,23,24)	6	3	3	2
Lipase increased - Grade 4(n=38,15,23,24)	2	0	2	0
Serum amylase increased - Grade 3(n=32,14,18,22)	2	1	1	0
Serum amylase increased - Grade 4(n=32,14,18,22)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Achieving a CR/CRi with Minimal Residual Disease (MRD) Negativity

End point title	Number of Subjects Achieving a CR/CRi with Minimal Residual Disease (MRD) Negativity[10]

End point description:

Subjects who achieved CR/CRi, a patient was considered to be MRD negative if the minimum MRD (%) between the date of achieving CR/CRi and end of treatment test is <0.01%. All subjects who were randomised into the study and achieved CR/CRi.

End point type	Secondary

End point timeframe:

At screening, once at Day 16-28 of Cycles 1 and 2, or until CR/CRi and MRD negativity were achieved, then after every 1-2 cycles as clinically indicated, and at EOT visit

Notes:

[10] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	46	11	35	26
Units: Subjects	33	8	25	18

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Remission (DoR) in Subjects who Achieved CR/CRi

End point title	Duration of Remission (DoR) in Subjects who Achieved

End point description:

DoR was defined as time from date of first response in responders (CR/CRi) to the date of disease progression (i.e., objective progression, relapse from CR/CRi, including post-study treatment follow-up disease assessments) or death due to any cause, whichever occurs first. DoR was estimated using Kaplan-Meier methods. 99999 indicates upper limit was not estimated due to fewer number of subjects with event. Subjects who were randomised into the study and with a remission (CR/CRi).

End point type	Secondary

End point timeframe:

From date of first response (subjects who achieved CR/CRi) to the date of disease progression or death due to any cause

Notes:

[11] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	46	11	35	26
Units: Months				
median (confidence interval 95%)	5.5 (4.7 to 13.4)	5.2 (1.9 to 99999)	6.5 (4.6 to 20.9)	6.8 (4.7 to 8.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Received HSCT Post Inotuzumab Ozogamicin Treatment

End point title	Number of Subjects who Received HSCT Post Inotuzumab Ozogamicin Treatment[12]

End point description:

Subjects who underwent HSCT after inotuzumab ozogamicin treatment. All subjects who were randomised into the study with study drug assignment based on randomisation.

End point type	Secondary

End point timeframe:

From first dose of study treatment till follow-up of up to 2 years

Notes:

[12] - 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: No statistical analysis was planned for this endpoint

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Subjects	31	10	21	12

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival[13]

End point description:

Overall survival was defined as the time from date of first dose of study treatment to death due to any cause. Subjects without confirmation of death were censored at the date that the subject was last known to be alive. 99999 indicates upper limit was not estimable due to fewer number of subjects with event. All subjects who were randomised into the study with study drug assignment based on randomisation.

End point type	Secondary

End point timeframe:

From date of randomisation to death due to any cause

Notes:

[13] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Months				
median (confidence interval 95%)	7.6 (5.8 to 10.0)	4.5 (3.2 to 8.6)	9.6 (6.4 to 99999)	8.1 (5.4 to 10.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)[14]

End point description:

PFS was defined as time from date of randomisation to the date of disease progression (i.e., objective progression, relapse from CR/CRi, including post-study treatment follow-up disease assessments), death due to any cause, or starting new induction therapy/post-therapy HSCT without achieving CR/CRi, whichever occurred first. PFS was estimated using Kaplan-Meier methods. Results were reported as of the data cutoff date on 21 Sep 2022.All subjects who were randomised into the study with study drug assignment based on randomisation.

End point type	Secondary

End point timeframe:

From date of randomisation to date of disease progression, death, or starting new induction therapy/post-therapy HSCT without achieving CR/Cri

Notes:

[14] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Months				
median (confidence interval 95%)	5.3 (3.4 to 7.2)	2.9 (1.7 to 5.8)	6.4 (4.8 to 16.0)	6.3 (2.8 to 8.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence Rate of Post-HSCT Relapse at Month 12

End point title	Cumulative Incidence Rate of Post-HSCT Relapse at Month

End point description:

Post-HSCT relapse is defined as the time from date of first HSCT after inotuzumab ozogamicin treatment to the date of first relapse post-HSCT. Cumulative incidence rates of an event at a particular timepoint were estimated with the CI calculated based on the cumulative incidence function using the method described by Kalbfleisch RL and Prentice JD. All subjects who were randomised into the study with study drug assignment based on randomisation and who were post HSCT.

End point type	Secondary

End point timeframe:

From date of HSCT to the date of first relapse post-HSCT to Month 12

Notes:

[15] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	10	21	12
Units: Percentages of subjects				
number (confidence interval 95%)	17.58 (6.17 to 33.79)	11.11 (0.40 to 41.66)	20.51 (6.00 to 40.97)	16.67 (2.26 to 42.89)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Post-HSCT Mortality

End point title	Number of Subjects With Post-HSCT Mortality[16]

End point description:

Post-HSCT Mortality was defined as the time from date of first HSCT after inotuzumab ozogamicin treatment to death due to any cause. All subjects who were randomised into the study with study drug assignment based on randomisation and who were post HSCT.

End point type	Secondary

End point timeframe:

From date of HSCT to the date of death due to any cause (approximately 4 years)

Notes:

[16] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	10	21	12
Units: Subjects	14	6	8	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Post HSCT non-Relapse Mortality

End point title	Number of Subjects With Post HSCT non-Relapse Mortality[17]

End point description:

Post HSCT non-relapse mortality was defined as time from date of first HSCT after inotuzumab ozogamicin treatment to death due to any cause without prior relapse. All subjects who were randomised into the study with study drug assignment based on randomisation and who underwent HSCT after inotuzumab ozogamicin treatment.

End point type	Secondary

End point timeframe:

From date of HSCT to the date of death due to any cause without prior relapse/progression post-HSCT (approximately 4 years)

Notes:

[17] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	10	21	12
Units: Subjects	10	5	5	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Post HSCT Relapse-Related Mortality

End point title	Number of Subjects with Post HSCT Relapse-Related

End point description:

Post HSCT Relapse-Related Mortality was defined as time from date of first HSCT after inotuzumab ozogamicin treatment to death due to any cause with prior relapse. All subjects who were randomised into the study with study drug assignment based on randomisation and who underwent HSCT after inotuzumab ozogamicin treatment.

End point type	Secondary

End point timeframe:

From date of HSCT to the date of death due to any cause with prior relapse/progression post-HSCT (approximately 4 years)

Notes:

[18] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.2 mg/m²/cycle (Dose Level 2 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	10	21	12
Units: Subjects	4	1	3	2

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Predose Concentrations (Ctrough) of Inotuzumab Ozogamicin

End point title	Mean Predose Concentrations (Ctrough) of Inotuzumab Ozogamicin[19]

End point description:

Ctrough was defined as the mean Predose concentration of study treatment. All treated subjects who received at least 1 dose of study drug and had at least one PK sample collected and analysed. 'Number analysed' = Subjects evaluable for this endpoint for each specified row.

End point type	Secondary

End point timeframe:

Pre-dose on Cycle 1 Day 1, 8 and 15, and on Day1 and 8 of Cycle 2, 3 and 4.

Notes:

[19] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	22	42	38
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (C1D1) n=61,22,39,37	0.8 (± 5.56)	1.9 (± 9.10)	0.2 (± 1.38)	0.1 (± 0.35)
C1D8 (n=60,22,38,36)	8.1 (± 21.24)	7.7 (± 20.53)	8.3 (± 21.91)	4.3 (± 6.05)
C1D15 (n=60,21,39,33)	15.8 (± 31.34)	8.9 (± 11.14)	19.5 (± 37.67)	25.8 (± 32.89)
C2D1 (n=54,17,37,24)	15.6 (± 24.95)	16.4 (± 21.43)	15.2 (± 26.67)	22.0 (± 47.15)
C2D8 (n=51,18,33,22)	42.7 (± 46.93)	42.6 (± 56.57)	42.8 (± 41.73)	48.6 (± 24.99)
C3D1 (n=17,5,12,11)	30.2 (± 43.39)	21.4 (± 18.46)	33.9 (± 50.64)	37.1 (± 34.03)
C3D8 (n=19,5,14,9)	36.2 (± 18.20)	31.9 (± 25.43)	37.8 (± 15.82)	68.8 (± 39.22)
C4D1 (n=6,2,4,0)	29.4 (± 18.12)	50.0 (± 14.64)	19.2 (± 7.42)	99999 (± 99999)
C4D8 (n=6,2,4,1	47.7 (± 10.63)	48.7 (± 7.99)	47.2 (± 12.88)	90.4 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-Drug Antibody (ADA)

End point title	Number of Subjects With Positive Anti-Drug Antibody (ADA)[20]

End point description:

ADA incidence is defined as combined results of treatment-boosted and treatment-induced ADA-positive subjects. The immunogenicity of inotuzumab ozogamicin was evaluated using a validated electrochemiluminescence (ECL)-based immunoassay. Subjects who received at least 1 dose of study drug and had at least 1 ADA sample collected and analysed for immunogenicity.

End point type	Secondary

End point timeframe:

At Day 1 of every cycle prior to the beginning of inotuzumab ozogamicin infusion and at the EOT visit, up to approximately 4 years

Notes:

[20] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.8 mg/m²/cycle (Dose Level 1 Randomised)	1.2 mg/m²/cycle (Dose Level 2 Randomized)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	63	22	38	41
Units: Subjects				
Positive Predose ADA	4	1	2	3
Treatment-induced ADA	1	1	1	0
Treatment-boosted ADA	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Neutralizing Antibody (NAb)

End point title	Number of Subjects With Positive Neutralizing Antibody

End point description:

NAb incidence is defined as combined results of treatment-boosted and treatment-induced NAb-positive subjects. The immunogenicity of inotuzumab ozogamicin was evaluated using a validated electrochemiluminescence (ECL)-based immunoassay. Subjects who received at least 1 dose of study drug and had at least 1 Nab sample collected and analysed for immunogenicity.

End point type	Secondary

End point timeframe:

At Day 1 of every cycle prior to the beginning of inotuzumab ozogamicin infusion and at the EOT visit, up to approximately 4 years.

Notes:

[21] - 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 descriptive analysis was planned for this endpoint.

End point values	1.2 mg/m²/cycle (Dose Level 2 Run-in + Randomized)	1.2 mg/m²/cycle (Dose Level 2 Run-in)	1.2 mg/m²/cycle (Dose Level 2 Randomised Phase)	1.8 mg/m²/cycle (Dose Level 1 Randomised)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	3	3
Units: Subjects				
Positive Predose NAb	0	0	0	0
Treatment-induced NAb	0	0	0	0
Treatment-boosted NAb	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of consent including a minimum of 9 weeks after the last dose

Adverse event reporting additional description:

Same event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as non-serious in another, or a participant may have experienced both a serious and non-serious event. Analysis performed on safety set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	1.2 mg/m2/cycle (Run-in)

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day1, 0.3 mg/m² on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

Reporting group title	1.8 mg/m2/cycle (Randomized)

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m²/cycle (0.8 mg/m² on Day 1, 0.5 mg/m² on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

Reporting group title	1.2 mg/m2/cycle (Run-in + Randomized)

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.8 mg/m² on Day 1, 0.5 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m²/cycle (0.5 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

Reporting group title	1.2 mg/m2/cycle (Randomized)

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m²/cycle administrated in 3 divided doses (0.6 mg/m² on Day 1, 0.3 mg/m² on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 0.9 mg/m²/cycle (0.3 mg/m² on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

Serious adverse events	1.2 mg/m2/cycle (Run-in)	1.8 mg/m2/cycle (Randomized)	1.2 mg/m2/cycle (Run-in + Randomized)
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 22 (68.18%)	21 / 38 (55.26%)	43 / 64 (67.19%)
number of deaths (all causes)	16	26	40
number of deaths resulting from adverse events	7	10	19
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm recurrence			

subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 22 (0.00%)	2 / 38 (5.26%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	3 / 22 (13.64%)	2 / 38 (5.26%)	4 / 64 (6.25%)
occurrences causally related to treatment / all	0 / 3	2 / 4	0 / 4
deaths causally related to treatment / all	0 / 2	1 / 2	0 / 3
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	3 / 38 (7.89%)	3 / 64 (4.69%)
occurrences causally related to treatment / all	0 / 1	2 / 3	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1
Immune system disorders			
Graft versus host disease in liver			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Sinus polyp			

subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella test positive			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Post procedural inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Cardiac disorders			
Coronary artery thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Central nervous system lesion			

subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 22 (0.00%)	2 / 38 (5.26%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	3 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Blood and lymphatic system disorders			
Anaemia megaloblastic			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	3 / 22 (13.64%)	4 / 38 (10.53%)	7 / 64 (10.94%)
occurrences causally related to treatment / all	4 / 4	4 / 6	7 / 8
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Enterocolitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Venoocclusive liver disease			
subjects affected / exposed	2 / 22 (9.09%)	2 / 38 (5.26%)	8 / 64 (12.50%)
occurrences causally related to treatment / all	5 / 5	1 / 2	6 / 12
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 2
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
COVID-19			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

COVID-19 pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	3 / 64 (4.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Hepatosplenic candidiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	2 / 22 (9.09%)	0 / 38 (0.00%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal sepsis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cellulitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Klebsiella sepsis			

subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Septic shock			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	4 / 64 (6.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 3
Sepsis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 38 (2.63%)	6 / 64 (9.38%)
occurrences causally related to treatment / all	0 / 3	2 / 2	0 / 8
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 4
Pneumonia klebsiella			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 2
Pneumonia fungal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pneumonia			

subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Urinary tract infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 38 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	0 / 64 (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
Tumour lysis syndrome			
subjects affected / exposed	1 / 22 (4.55%)	3 / 38 (7.89%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	1.2 mg/m2/cycle (Randomized)		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 42 (66.67%)		
number of deaths (all causes)	24		
number of deaths resulting from adverse events	12		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm recurrence			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasm progression			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Graft versus host disease in liver			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Sinus polyp			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Klebsiella test positive			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural inflammation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery thrombosis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Central nervous system lesion			

subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Focal dyscognitive seizures				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia megaloblastic				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	4 / 42 (9.52%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Pancreatitis acute				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				

subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Venoocclusive liver disease			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
COVID-19			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

COVID-19 pneumonia				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 2			
Hepatosplenic candidiasis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fungal infection				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fungal sepsis				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella sepsis				

subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Infection				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Septic shock				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
Sepsis				
subjects affected / exposed	4 / 42 (9.52%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 3			
Pneumonia klebsiella				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Pneumonia fungal				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	0 / 42 (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	1.2 mg/m2/cycle (Run-in)	1.8 mg/m2/cycle (Randomized)	1.2 mg/m2/cycle (Run-in + Randomized)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 22 (81.82%)	29 / 38 (76.32%)	50 / 64 (78.13%)
Investigations			
Platelet count decreased			
subjects affected / exposed	3 / 22 (13.64%)	3 / 38 (7.89%)	3 / 64 (4.69%)
occurrences (all)	3	12	3
Neutrophil count decreased			
subjects affected / exposed	4 / 22 (18.18%)	4 / 38 (10.53%)	5 / 64 (7.81%)
occurrences (all)	9	17	15
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 22 (4.55%)	6 / 38 (15.79%)	5 / 64 (7.81%)
occurrences (all)	1	6	6
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 22 (9.09%)	4 / 38 (10.53%)	5 / 64 (7.81%)
occurrences (all)	2	4	5
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 22 (4.55%)	3 / 38 (7.89%)	3 / 64 (4.69%)
occurrences (all)	2	3	5
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 22 (18.18%)	8 / 38 (21.05%)	7 / 64 (10.94%)
occurrences (all)	7	10	11
Alanine aminotransferase increased			
subjects affected / exposed	5 / 22 (22.73%)	3 / 38 (7.89%)	10 / 64 (15.63%)
occurrences (all)	8	6	14
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 22 (0.00%)	2 / 38 (5.26%)	2 / 64 (3.13%)
occurrences (all)	0	2	2
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 22 (9.09%)	0 / 38 (0.00%)	2 / 64 (3.13%)
occurrences (all)	2	0	2
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 22 (0.00%)	4 / 38 (10.53%)	4 / 64 (6.25%)
occurrences (all)	0	4	4
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	5 / 22 (22.73%)	13 / 38 (34.21%)	19 / 64 (29.69%)
occurrences (all)	10	29	40
Leukopenia			
subjects affected / exposed	2 / 22 (9.09%)	6 / 38 (15.79%)	8 / 64 (12.50%)
occurrences (all)	3	10	9
Febrile neutropenia			
subjects affected / exposed	1 / 22 (4.55%)	4 / 38 (10.53%)	3 / 64 (4.69%)
occurrences (all)	1	5	4
Anaemia			
subjects affected / exposed	2 / 22 (9.09%)	6 / 38 (15.79%)	11 / 64 (17.19%)
occurrences (all)	6	9	23
Neutropenia			
subjects affected / exposed	4 / 22 (18.18%)	10 / 38 (26.32%)	20 / 64 (31.25%)
occurrences (all)	6	26	43
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 22 (22.73%)	1 / 38 (2.63%)	10 / 64 (15.63%)
occurrences (all)	13	1	22
Fatigue			
subjects affected / exposed	2 / 22 (9.09%)	1 / 38 (2.63%)	4 / 64 (6.25%)
occurrences (all)	2	1	4
Asthenia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 38 (5.26%)	1 / 64 (1.56%)
occurrences (all)	0	3	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 22 (4.55%)	4 / 38 (10.53%)	3 / 64 (4.69%)
occurrences (all)	2	4	4
Abdominal pain upper			
subjects affected / exposed	0 / 22 (0.00%)	3 / 38 (7.89%)	1 / 64 (1.56%)
occurrences (all)	0	3	1

Abdominal pain			
subjects affected / exposed	2 / 22 (9.09%)	1 / 38 (2.63%)	7 / 64 (10.94%)
occurrences (all)	3	1	8
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 38 (2.63%)	3 / 64 (4.69%)
occurrences (all)	0	1	4
Vomiting			
subjects affected / exposed	1 / 22 (4.55%)	3 / 38 (7.89%)	6 / 64 (9.38%)
occurrences (all)	2	5	9
Stomatitis			
subjects affected / exposed	1 / 22 (4.55%)	2 / 38 (5.26%)	2 / 64 (3.13%)
occurrences (all)	1	4	2
Nausea			
subjects affected / exposed	0 / 22 (0.00%)	3 / 38 (7.89%)	5 / 64 (7.81%)
occurrences (all)	0	4	5
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 22 (13.64%)	4 / 38 (10.53%)	5 / 64 (7.81%)
occurrences (all)	4	4	7
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	1 / 22 (4.55%)	2 / 38 (5.26%)	1 / 64 (1.56%)
occurrences (all)	1	2	1
Pruritus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 38 (0.00%)	3 / 64 (4.69%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	2 / 38 (5.26%)	1 / 64 (1.56%)
occurrences (all)	0	2	1
Bone pain			
subjects affected / exposed	0 / 22 (0.00%)	3 / 38 (7.89%)	1 / 64 (1.56%)
occurrences (all)	0	4	1
Infections and infestations			
Pneumonia			

subjects affected / exposed	3 / 22 (13.64%)	0 / 38 (0.00%)	4 / 64 (6.25%)
occurrences (all)	3	0	4
Influenza			
subjects affected / exposed	2 / 22 (9.09%)	0 / 38 (0.00%)	2 / 64 (3.13%)
occurrences (all)	2	0	2
Urinary tract infection			
subjects affected / exposed	0 / 22 (0.00%)	2 / 38 (5.26%)	2 / 64 (3.13%)
occurrences (all)	0	2	2
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 38 (2.63%)	4 / 64 (6.25%)
occurrences (all)	2	1	6
Hypomagnesaemia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 38 (2.63%)	4 / 64 (6.25%)
occurrences (all)	1	1	5

Non-serious adverse events	1.2 mg/m2/cycle (Randomized)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 42 (76.19%)		
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	6		
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Aspartate aminotransferase			

increased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Alanine aminotransferase increased			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	30		
Leukopenia			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Febrile neutropenia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Anaemia			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	17		
Neutropenia			
subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	37		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	5 / 42 (11.90%) 9 2 / 42 (4.76%) 2 1 / 42 (2.38%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 2 1 / 42 (2.38%) 1 5 / 42 (11.90%) 5 3 / 42 (7.14%) 4 5 / 42 (11.90%) 7 1 / 42 (2.38%) 1 5 / 42 (11.90%) 5		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 3		
Skin and subcutaneous tissue disorders			

Rash papular subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0 3 / 42 (7.14%) 3		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all)	 1 / 42 (2.38%) 1 1 / 42 (2.38%) 1		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 1 / 42 (2.38%) 1 0 / 42 (0.00%) 0 2 / 42 (4.76%) 2		
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 4 3 / 42 (7.14%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported