Clinical trial results:
A Phase 1b/2 Study of the Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of the Selective SYK Inhibitor Lanraplenib (LANRA) in Combination with the FLT3 Inhibitor Gilteritinib, in Patients with FLT3-mutated Relapsed or Refractory AML

Summary

EudraCT number	2022-001279-15
Trial protocol	ES
Global end of trial date	09 April 2024

Results information

Result version number	v1 (current)
This version publication date	27 July 2024
First version publication date	27 July 2024

Trial information

Trial identification

Sponsor protocol code	KB-LANRA-1001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05028751
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 156759

Notes:

Sponsors

Sponsor organisation name	Kronos Bio, Inc.
Sponsor organisation address	1300 So. El Camino Real, Suite 400, San Mateo, CA, United States, 94402
Public contact	VP, Corporate Affairs,, Kronos Bio, Inc., +1 16507815200, media@kronosbio.com
Scientific contact	VP, Corporate Affairs,, Kronos Bio, Inc., +1 16507815200, media@kronosbio.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	09 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

For Phase 1b: To evaluate the safety of LANRA in combination with the FMS-like tyrosine kinase 3 (FLT3) inhibitor gilteritinib, in participants with relapsed/refractory (R/R) FLT3-mutated AML.
For Phase 2: To further evaluate the safety of LANRA at its recommended Phase 2 dose (RP2D) in combination with gilteritinib in participants with FLT3-mutated AML.

Protection of trial subjects:

The investigator ensured that this study was conducted in accordance with the principles of the Declaration of Helsinki, International Council for Harmonisation (ICH) Good Clinical Practice (GCP), and other country-specific requirements, as applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 August 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	24
EEA total number of subjects	12

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)	6
From 65 to 84 years	18

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 24 participants were enrolled at sites in the United States and Europe.

Pre-assignment

Screening details:

A total of 35 participants were screened, of which 24 participants were enrolled and received study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LANRA 20 mg QD + Gilteritinib 120 mg QD

Arm description:

Participants received LANRA 20 mg once daily (QD) as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a partial remission (PR) after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Arm type	Experimental
Investigational medicinal product name	LANRA
Investigational medicinal product code	
Other name	Lanraplenib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg QD oral tablets.

Investigational medicinal product name	Gilteritinib
Investigational medicinal product code	
Other name	Xospata
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg QD oral tablets.

Arm title	LANRA 40 mg QD + Gilteritinib 120 mg QD

Arm description:

Participants received LANRA 40 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Arm type	Experimental
Investigational medicinal product name	LANRA
Investigational medicinal product code	
Other name	Lanraplenib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details: 40 mg QD oral tablets.	
Investigational medicinal product name	Gilteritinib
Investigational medicinal product code	
Other name	Xospata
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 120 mg QD oral tablets.	
Arm title	LANRA 60 mg QD + Gilteritinib 120 mg QD

Arm description:

Participants received LANRA 60 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Arm type	Experimental
Investigational medicinal product name	LANRA
Investigational medicinal product code	
Other name	Lanraplenib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 60 mg QD oral tablets.	
Investigational medicinal product name	Gilteritinib
Investigational medicinal product code	
Other name	Xospata
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 120 mg QD oral tablets.	
Arm title	LANRA 90 mg QD + Gilteritinib 120 mg QD

Arm description:

Participants received LANRA 90 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Arm type	Experimental
Investigational medicinal product name	LANRA
Investigational medicinal product code	
Other name	Lanraplenib
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 90 mg QD oral tablets.	
Investigational medicinal product name	Gilteritinib
Investigational medicinal product code	
Other name	Xospata
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 120 mg QD oral tablets.	

Number of subjects in period 1	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD
Started	14	3	3
Completed	0	0	0
Not completed	14	3	3
Consent withdrawn by subject	-	-	1
Death	9	3	2
Miscellaneous	2	-	-
Study terminated by sponsor	3	-	-

Number of subjects in period 1	LANRA 90 mg QD + Gilteritinib 120 mg QD
Started	4
Completed	0
Not completed	4
Consent withdrawn by subject	-
Death	4
Miscellaneous	-
Study terminated by sponsor	-

Baseline characteristics

Reporting groups	
Reporting group title	LANRA 20 mg QD + Gilteritinib 120 mg QD
Reporting group description:	
Participants received LANRA 20 mg once daily (QD) as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a partial remission (PR) after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.	
Reporting group title	LANRA 40 mg QD + Gilteritinib 120 mg QD
Reporting group description:	
Participants received LANRA 40 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.	
Reporting group title	LANRA 60 mg QD + Gilteritinib 120 mg QD
Reporting group description:	
Participants received LANRA 60 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.	
Reporting group title	LANRA 90 mg QD + Gilteritinib 120 mg QD
Reporting group description:	
Participants received LANRA 90 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.	

Reporting group values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD
Number of subjects	14	3	3
Age categorical Units: Subjects			
Adults (18-64 years)	3	2	1
From 65-84 years	11	1	2
Age continuous Units: years			
arithmetic mean	67.9	54.0	70.0
standard deviation	± 19.00	± 16.82	± 13.45
Gender categorical Units: Subjects			
Female	5	1	1
Male	9	2	2
Race/Ethnicity Units: Subjects			
White	13	2	3
Not Reported	1	0	0
Other	0	1	0
Ethnicity			

Units: Subjects			
Hispanic or Latino	3	2	0
Not Hispanic or Latino	8	1	3
Unknown or Not Reported	3	0	0

Reporting group values	LANRA 90 mg QD + Gilteritinib 120 mg QD	Total	
Number of subjects	4	24	
Age categorical Units: Subjects			
Adults (18-64 years)	0	6	
From 65-84 years	4	18	
Age continuous Units: years			
arithmetic mean	74.3		
standard deviation	± 3.69	-	
Gender categorical Units: Subjects			
Female	2	9	
Male	2	15	
Race/Ethnicity Units: Subjects			
White	4	22	
Not Reported	0	1	
Other	0	1	
Ethnicity Units: Subjects			
Hispanic or Latino	1	6	
Not Hispanic or Latino	3	15	
Unknown or Not Reported	0	3	

End points reporting groups

Reporting group title	LANRA 20 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 20 mg once daily (QD) as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a partial remission (PR) after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Reporting group title	LANRA 40 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 40 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Reporting group title	LANRA 60 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 60 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Reporting group title	LANRA 90 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 90 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Subject analysis set title	LANRA QD + Gilteritinib 120 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received LANRA QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Primary: Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)[1]

End point description:

A TEAE was any unfavorable or unintended sign, symptom, laboratory abnormality or disease (new or exacerbated) temporally associated with the use of a study drug, whether considered causally related to the study drug or not that started after the first dose of the earliest study drug through the lesser of non-protocol anti-leukemic therapy initiation or end of treatment visit.

A serious TEAE was defined as any TEAE that:
• Resulted in death.
• Was life-threatening.
• Required or prolonged a pre-existing hospitalization.
• Resulted in disability/incapacity.
• Was a congenital anomaly/birth defect.
• Was considered a significant medical event by the investigator.

Safety Population: Consisted of all participants who received ≥ 1 dose of either study drug and had at least 1 on-treatment safety-related observation.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 (each cycle was 28 days) to 30 days after last dose of either LANRA or gilteritinib or initiation of non-protocol antileukemic therapy, whichever was earlier (maximum duration of treatment was 183 days)

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 comparative statistical analyses were planned.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	3	3	4
Units: participants				
TEAEs	14	3	3	4
TESAEs	11	3	3	4
Grade 3 or Grade 4 TEAEs	12	3	2	3
AEs Leading to Death (Grade 5)	2	0	1	4
TEAEs Related to LANRA	5	0	1	0
TEAEs Related to Gilteritinib	8	0	1	0
TEAEs Leading to Dose Reduction of LANRA	0	0	0	0
TEAEs Leading to Dose Reduction of Gilteritinib	0	0	0	0
TEAEs Leading to LANRA Interruption	9	0	0	2
TEAEs Leading to Gilteritinib Interruption	9	0	0	2
TEAEs Leading to LANRA Discontinuation	1	0	1	2
TEAEs Leading to Gilteritinib Discontinuation	1	0	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Dose-limiting Toxicity (DLT) for LANRA

End point title	Number of Participants Who Experienced a Dose-limiting Toxicity (DLT) for LANRA[2]

End point description:

A DLT was defined as any of the following occurring within the DLT assessment period:
• A nonhematologic toxicity of Grade ≥ 3 that was at least possibly related to LANRA (with noted exceptions).
• Any toxicity that resulted in administration of < 80% of the cumulative, Cycle 1 dose for either LANRA or gilteritinib.
• Grade 4 neutropenia or thrombocytopenia lasting > 28 days after treatment onset that was not attributed to AML and was at least possibly related to LANRA.
• Any toxicity that resulted in reduction in the dose of LANRA in Cycle 1. TEAEs were graded for severity based on the NCI-CTCAE version 5.0 as follows:
• Grade 3 - Severe.
• Grade 4 - Life-threatening.

Safety Population: Consisted of all participants who received ≥ 1 dose of either study drug and had at

least 1 on-treatment safety-related observation.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to pre-dose Cycle 2 Day 1 (each cycle was 28 days)

Notes:

[2] - 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 comparative statistical analyses were planned.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	3	3	4
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Maximally Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D) of LANRA in Combination With Standard Doses of Gilteritinib

End point title	Maximally Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D) of LANRA in Combination With Standard Doses of Gilteritinib[3]

End point description:

The MTD/RP2D was defined as the highest dose with either 0 of 3 or no more than 1 of 6 patients with LANRA-related DLTs. All decisions regarding dose escalation including declaration of the MTD/RP2D were made by the dose-escalation committee (DEC).

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to pre-dose Cycle 2 Day 1 (each cycle was 28 days)

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 comparative statistical analyses were planned.

End point values	LANRA QD + Gilteritinib 120 mg QD			
Subject group type	Subject analysis set			
Number of subjects analysed	0[4]			
Units: mg				
number (not applicable)				

Notes:

[4] - The study was terminated before MTD/RP2D could be determined.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximal Plasma Concentration (Cmax) of LANRA

End point title	Maximal Plasma Concentration (Cmax) of LANRA

End point description:

Cmax was derived from plasma concentrations of LANRA using standard non-compartmental methods and actual sample times.

Pharmacokinetic (PK) Population: Consisted of all participants with at least 1 post-dose LANRA plasma concentration with available data at each PK assessment time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 1 Day 15: Pre-dose and 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	4[5]
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1	148 (± 59.7)	340 (± 277)	441 (± 146)	694 (± 242)
Cycle 1 Day 15	181 (± 41.3)	298 (± 111)	591 (± 112)	597 (± 65.1)

Notes:

[5] - Cycle 1 Day 15 N = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax (Tmax) of LANRA

End point title	Time to Cmax (Tmax) of LANRA

End point description:

Tmax was derived from plasma concentrations of LANRA using standard non-compartmental methods and actual sample times.

PK Population: Consisted of all participants with at least 1 post-dose LANRA plasma concentration with available data at each PK assessment time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 1 Day 15: Pre-dose and 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	4[6]
Units: hours				
arithmetic mean (standard deviation)				

Cycle 1 Day 1	2.2 (± 1.3)	3.5 (± 2.78)	3.33 (± 2.31)	2.5 (± 1.29)
Cycle 1 Day 15	2.8 (± 0.837)	2.0 (± 0.0)	2.0 (± 1.0)	3.0 (± 1.4)

Notes:

[6] - Cycle 1 Day 15 N = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Area of the Plasma Concentration x Time Curve From Hour 0 to the Last Measurable Time Point (AUC0-last) of LANRA

End point title	Area of the Plasma Concentration x Time Curve From Hour 0 to the Last Measurable Time Point (AUC0-last) of LANRA

End point description:

AUC0-last was derived from plasma concentrations of LANRA using standard non-compartmental methods and actual sample times.

PK Population: Consisted of all participants with at least 1 post-dose LANRA plasma concentration with available data at each PK assessment time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 1 Day 15: Pre-dose and 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	4[7]
Units: h*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1	1600 (± 462)	3100 (± 1920)	5240 (± 1550)	7700 (± 1520)
Cycle 1 Day 15	2510 (± 557)	3320 (± 1100)	8430 (± 1860)	8490 (± 1360)

Notes:

[7] - Cycle 1 Day 15 N = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Gilteritinib

End point title	Cmax of Gilteritinib

End point description:

Cmax was derived from plasma concentrations of gilteritinib using standard non-compartmental methods and actual sample times.

PK Population: Consisted of all participants with at least 1 post-dose gilteritinib plasma concentration with available data at each PK assessment time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 15: Pre-dose and 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	2
Units: ng/mL				
arithmetic mean (standard deviation)	434 (± 130)	621 (± 392)	352 (± 198)	326 (± 168)

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of Gilteritinib

End point title	Tmax of Gilteritinib

End point description:

Tmax was derived from plasma concentrations of gilteritinib using standard non-compartmental methods and actual sample times.

PK Population: Consisted of all participants with at least 1 post-dose gilteritinib plasma concentration with available data at each PK assessment time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 15: Pre-dose and 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	2
Units: hours				
arithmetic mean (standard deviation)	5.8 (± 2.28)	3 (± 2.65)	5 (± 2.65)	5.5 (± 3.54)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-last of Gilteritinib

End point title	AUC0-last of Gilteritinib

End point description:

AUC0-last was derived from plasma concentrations of gilteritinib using standard non-compartmental methods and actual sample times.

PK Population: Consisted of all participants with at least 1 post-dose gilteritinib plasma concentration with available data at each PK assessment time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 15: Pre-dose and 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose.

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	2
Units: h*ng/mL				
arithmetic mean (standard deviation)	8610 (± 2630)	12100 (± 8200)	7460 (± 4870)	6390 (± 3060)

Statistical analyses

No statistical analyses for this end point

Secondary: Composite Complete Remission (cCR) Rate Per European LeukemiaNet (ELN) 2017 Criteria

End point title	Composite Complete Remission (cCR) Rate Per European LeukemiaNet (ELN) 2017 Criteria

End point description:

Percentage of participants with cCR included CR and CR with partial hematologic recovery (CRh).

CR required all of the following, per ELN 2017 criteria:
- Bone marrow blasts < 5 %.
- Absence of circulating blasts and blasts with Auer rods.
- Absence of extramedullary disease (ie, leukemia outside of bone marrow confirmed by biopsy).
- Absolute neutrophil count > 1.0 x 10^9/L (1,000/µL).
- Platelet count >100 x 10^9/L (100,000/µL).

CRh required all aforementioned CR criteria except for the below:
- Absolute neutrophil count > 0.5 x 10^9/L (500/µL) and/or;
- Platelet count > 50 x 10^9/L (50,000/µL).

Efficacy Evaluable Population: Consisted of all participants who received ≥1 dose of either study drug and completed the first protocol-specified response assessment or discontinued study treatment for toxicity or died prior to the first response assessment. Participants with no post-baseline response assessments were considered non-responders.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 until occurrence of documented CR or CRh (maximum duration of follow-up was 16.1 months).

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	3	3	4
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 24.7)	0 (0 to 70.8)	0 (0 to 70.8)	0 (0 to 60.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined as the time from first qualifying response (CR/CRh) until relapse or death from any cause, as assessed by study investigators.

CR required all of the following, per ELN 2017 criteria:
• Bone marrow blasts < 5 %.
• Absence of circulating blasts and blasts with Auer rods.
• Absence of extramedullary disease (ie, leukemia outside of bone marrow confirmed by biopsy).
• Absolute neutrophil count > 1.0 x 10^9/L (1,000/µL).
• Platelet count >100 x 10^9/L (100,000/µL).

CRh required all aforementioned CR criteria except for the below:
• Absolute neutrophil count > 0.5 x 10^9/L (500/µL) and/or;
• Platelet count > 50 x 10^9/L (50,000/µL).

Relapse was defined as the reappearance of circulating blasts or ≥ 5% blasts in the bone marrow not attributable to any other cause or reappearance of cytologically or biopsy documented extramedullary disease.

Efficacy Evaluable Population including only participants who had a CR/CRh.

End point type	Secondary

End point timeframe:

From first qualifying response (CR/CRh) until relapse or death from any cause (maximum duration of follow-up was 16.1 months).

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	0[9]	0[10]	0[11]
Units: months				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[8] - No participants had a CR/CRh so DOR was not estimable.

[9] - No participants had a CR/CRh so DOR was not estimable.

[10] - No participants had a CR/CRh so DOR was not estimable.

[11] - No participants had a CR/CRh so DOR was not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival (EFS)

End point title	Event-free Survival (EFS)

End point description:

EFS was defined as the time from treatment onset until treatment failure (ie, failure to achieve CR/CRh), relapse from CR/CRh, or death from any cause.

CR required all of the following:
• Bone marrow blasts < 5 %.
• Absence of circulating blasts and blasts with Auer rods.
• Absence of extramedullary disease (ie, leukemia outside of bone marrow confirmed by biopsy).
• Absolute neutrophil count > 1.0 x 10^9/L (1,000/µL).
• Platelet count >100 x 10^9/L (100,000/µL).

CRh required all aforementioned CR criteria except for the below:
• Absolute neutrophil count > 0.5 x 10^9/L (500/µL) and/or;
• Platelet count > 50 x 10^9/L (50,000/µL).

Relapse was defined as the reappearance of circulating blasts or ≥ 5% blasts in the bone marrow not attributable to any other cause or reappearance of cytologically or biopsy documented extramedullary disease.

Efficacy Evaluable Population.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 to treatment failure (ie, failure to achieve CR or CRh), relapse from CR/CRh or death from any cause (maximum duration of follow-up was 16.1 months).

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[12]	0[13]	0[14]	0[15]
Units: months				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[12] - No data was evaluable as no participants had a CR or CRh.

[13] - No data was evaluable as no participants had a CR or CRh.

[14] - No data was evaluable as no participants had a CR or CRh.

[15] - No data was evaluable as no participants had a CR or CRh.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from enrollment until death from any cause. Overall survival was estimated using Kaplan-Meier methodology.

9999.9 = Upper limit was not reached due to low number of events.

Safety Population: Consisted of all participants who received ≥ 1 dose of either study drug and had at least 1 on-treatment safety-related observation. Participants alive at last follow-up were censored at the date of last contact.

End point type	Secondary

End point timeframe:

Enrollment until death from any cause (maximum duration of follow-up was 16.1 months).

End point values	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD	LANRA 90 mg QD + Gilteritinib 120 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	3	3	4
Units: months				
median (confidence interval 95%)	4.0 (0.9 to 10.9)	2.6 (2.2 to 9999.9)	3.7 (1.5 to 9999.9)	0.5 (0.3 to 9999.9)

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Cycle 1 Day 1 to 30 days after last dose of either LANRA or gilteritinib or initiation of new, non-protocol, anti-leukemic therapy, if sooner. All-cause mortality: Enrollment to end of study.

Adverse event reporting additional description:

Safety Population: Consisted of all participants who received ≥ 1 dose of either study drug and had at least 1 on-treatment safety-related observation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	LANRA 20 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 20 mg once daily (QD) as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a partial remission (PR) after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Reporting group title	LANRA 40 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 40 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Reporting group title	LANRA 60 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 60 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Reporting group title	LANRA 90 mg QD + Gilteritinib 120 mg QD

Reporting group description:

Participants received LANRA 90 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 1. Participants also received gilteritinib 120 mg QD as oral tablets in consecutive 28-day cycles starting from Cycle 1 Day 2. Participants received treatment until progression/relapse or lack of at least a PR after 6 months of study treatment, intolerance, or withdrawal from treatment by the participant or study investigator.

Serious adverse events	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 14 (78.57%)	3 / 3 (100.00%)	3 / 3 (100.00%)
number of deaths (all causes)	9	3	2
number of deaths resulting from adverse events	2	0	1
Injury, poisoning and procedural complications			

Craniofacial fracture			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			

subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial mass			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	5 / 14 (35.71%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	1 / 8	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperleukocytosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Neutropenic colitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Enterocolitis infectious			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella bacteraemia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Pneumonia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia fungal			
subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Pneumonia staphylococcal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LANRA 90 mg QD + Gilteritinib 120 mg QD		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	4		

Injury, poisoning and procedural complications			
Craniofacial fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Superficial vein thrombosis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			

subjects affected / exposed	1 / 4 (25.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Intracranial mass				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ischaemic stroke				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Hyperleukocytosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pyrexia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Neutropenic colitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Acute febrile neutrophilic dermatosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bacteraemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterococcal bacteraemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterococcal infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella bacteraemia				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia fungal			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia staphylococcal			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Streptococcal bacteraemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 4 (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: 0 %

Non-serious adverse events	LANRA 20 mg QD + Gilteritinib 120 mg QD	LANRA 40 mg QD + Gilteritinib 120 mg QD	LANRA 60 mg QD + Gilteritinib 120 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Differentiation syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Catheter site pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chills			

subjects affected / exposed	4 / 14 (28.57%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Facial pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	3	0	4
Generalised oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Localised oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	3 / 14 (21.43%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	4	2	2
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Haemoptysis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tachypnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Depression			

subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphoria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 14 (28.57%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	5	0	3
Amylase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	3	0	3
Bilirubin conjugated increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Blood bilirubin increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Clostridium test positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
International normalised ratio increased			

subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	2
Lymphocyte count decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Pantoea agglomerans test positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	13	0	0
Troponin I increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
White blood cell count decreased			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	8	0	2
White blood cell count increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Face injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fall			

subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Subdural haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Transfusion reaction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Brain injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Dysgeusia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Hemiparesis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Lethargy			

subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	6	1	0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Leukopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lymphopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Splenic infarction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			

subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	4 / 14 (28.57%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	4	0	2
Dry mouth			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Gingival bleeding			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Melaena			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Skin mass			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Umbilical haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Chronic kidney disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Renal haemorrhage			

subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhabdomyolysis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Catheter site infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile colitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Enterobacter infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Enterococcal infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Enterovirus infection			

subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fungal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Perichondritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pneumonia klebsiella			
subjects affected / exposed	0 / 14 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Septic shock			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Hyperglycaemia			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Hypocalcaemia			
subjects affected / exposed	5 / 14 (35.71%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Hypokalaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hyponatraemia			
subjects affected / exposed	3 / 14 (21.43%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Non-serious adverse events	LANRA 90 mg QD + Gilteritinib 120 mg QD		
Total subjects affected by non-serious			

adverse events subjects affected / exposed	3 / 4 (75.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Differentiation syndrome subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0		
Vascular disorders Deep vein thrombosis subjects affected / exposed occurrences (all) Haematoma subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all) Orthostatic hypotension subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Catheter site pain subjects affected / exposed occurrences (all) Chest discomfort subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Facial pain	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Generalised oedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Localised oedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dysphoria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Bilirubin conjugated increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Clostridium test positive			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pantoea agglomerans test positive			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Troponin I increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
White blood cell count increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Face injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Subdural haematoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Transfusion reaction			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all) Supraventricular tachycardia subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Nervous system disorders Aphasia subjects affected / exposed occurrences (all) Brain injury subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hemiparesis subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Splenic infarction			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Diarrhoea			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gingival bleeding			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia oral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Melaena			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Alopecia			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin mass			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Umbilical haematoma			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chronic kidney disease			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Renal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rhabdomyolysis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Enterobacter infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Enterococcal bacteraemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Enterococcal infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Enterovirus infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nasopharyngitis			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Perichondritis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pneumonia klebsiella			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rhinovirus infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Hypernatraemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2		
Hyperphosphataemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2021	The following updates were made: • The starting dose of LANRA in Phase 1b was reduced from 30 mg QD to 20 mg QD. • A potential fourth dose cohort in Phase 1b was added. • The estimated study enrollment was increased to 55 participants (from 35 participants) to accommodate the potential fourth dose cohort and to allow greater statistical precision for the primary efficacy endpoint, composite CR (CR, CRh) rate. • A requirement was added that participants who had not achieved at least a PR after 6 months of study treatment must have permanently discontinued for lack of efficacy. • Criteria defining eligibility for renal function and left ventricular ejection fraction were modified. • Changes were made in the treatment modification guidelines for potential gilteritinib- or LANRA-related hematologic and non-hematologic toxicities. • Additional electrocardiograms (ECGs) timed to coincide with PK blood sampling were added. • Criteria for study treatment discontinuation were updated. • The requirement for cumulative treatment intensity of at least 80% for both study drugs in Cycle 1 as a condition of eligibility for DLT assessment in the absence of a DLT was added. Other changes to the DLT definition were made at the request of the Food and Drug Administration (FDA).
12 May 2022	The following updates were made: • The protocol was updated to reflect that the study is being conducted worldwide rather than only at US sites. • Eligibility was broadened to allow previous exposure to not only midostaurin or other multikinase inhibitors (eg, sorafenib) but also to gilteritinib or another selective FLT3 inhibitor, in order to expand the pool of eligible patients. • Updates were made to allow for interruption of treatment with LANRA in the event that treatment with a strong cytochrome P450 3A4 (CYP3A4) inhibitor was required. • Contraceptive guidance was revised to require the use of a condom or other barrier method, in addition to other highly effective methods of contraception. • A new section was added to provide brief context regarding the added risks associated with COVID-19 resulting from compromised immunity due to cancer chemotherapy and to reference the latest US and European Union (EU) guidelines for clinical trial conduct in the setting of the COVID-19 pandemic. • Clarifications were added to indicate the difference between initial doses of study medications in Phase 1b (LANRA only on C1D1) and Phase 2 (combination therapy starting from C1D1).

14 October 2022	The following updates were made: • Differentiation Syndrome (DS) was designated as an adverse event of special interest (AESI). • The DLT criteria for nonhematologic toxicity of Grade ≥ 3 was modified to exclude "manifestations of DS that are responsive within 48 hours to treatment with systemic high-dose steroids plus supportive care interventions including but not limited to: hemodynamic support; use of diuretics for management of fluid retention; uricolytic agents in participants at risk for tumor lysis syndrome; and hydroxyurea in participants with hyperleukocytosis without evidence of infection, either with or without interruption of study treatment." • The section on permitted medications was amended to allow intrathecal chemotherapy for prophylaxis against central nervous system (CNS) leukemia in accordance with institutional care standards.
17 November 2022	The following updates were made: • Revisions were made to clarify that both serious and non-serious DS events must be recorded promptly in the electronic data capture (EDC) system and reported promptly. • The DLT criteria for nonhematologic toxicity of Grade ≥ 3 was revised to exclude "Grade 3 or 4 DS … successfully managed with systemic high-dose steroids plus supportive care interventions with resolution within 7 days and without resulting end-organ damage."
31 March 2023	The following updates were made: • Allocation of participants to backfill cohorts was allowed to better understand the safety, tolerability, PK, pharmacodynamics (PD), and antitumor activity of the study regimen across multiple dose levels. • The overall enrollment estimate was increased to 100 participants (from 55 participants) to accommodate enrollment to backfill cohorts. • The Screening Phase was extended to 21 days to allow greater flexibility for the scheduling of screening assessments. • Changes were made to allow for treatment interruptions of up to 28 days for specified toxicities and to provide additional clarity regarding treatment modifications for hematologic toxicities. • Additional detail was added regarding study treatment discontinuation in the setting of toxicity (and in particular, chronic, low-grade cumulative toxicities) or non-compliance with the study regimen. • The summary of gilteritinib safety data was updated to align with the Summary of Product Characteristics, which was the reference safety information for the study.
30 May 2023	The following updates were made: • A requirement was added to indicate that backfill participants may be added only to cohort(s) with at least 1 of the 3 to 6 participants initially enrolled to that cohort having achieved a response of CR, CRh, complete remission with incomplete blood count recovery (CRi), PR, or morphologic leukemia-free state (MLFS). • Treatment interruptions for nonhematologic toxicities were limited to a maximum of 14 days.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

In light of the Sponsor’s decision to terminate the trial at completion of Phase 1b, all analyses were restricted to results from Phase 1b participants only. Phase 2 was not enrolled.

Notes: