



Clinical trial results:
Clinical Evaluation of 506U78 in Japanese Patients with Relapsed or Refractory T-cell Acute Lymphoblastic Leukemia or T-cell Lymphoblastic Lymphoma
Summary

EudraCT number	2015-004902-41
Trial protocol	Outside EU/EEA
Global end of trial date	15 July 2009

Results information

Result version number	v1 (current)
This version publication date	29 January 2017
First version publication date	29 January 2017

Trial information

Trial identification

Sponsor protocol code	PGA105446
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 November 2009
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of nelarabine administered to Japanese participants with T-cell acute lymphoblastic leukemia (T-ALL) or T-cell lymphoblastic lymphoma (T-LBL) as a 2-hour intravenous infusion on a Day 1, 3 and 5 schedule for adult participants and as a 1-hour infusion on a Days 1-5 schedule for pediatric participants.

To determine the plasma pharmacokinetic (PK) profiles of nelarabine and 9-beta-D-arabinofuranosyl guanine (ara-G) when nelarabine is administered on these schedules.

To determine intracellular ara-G triphosphate (ara-GTP) concentrations when nelarabine is administered on these schedules.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 August 2006
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	Japan: 13
Worldwide total number of subjects	13
EEA total number of subjects	0

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)	5
Adolescents (12-17 years)	5
Adults (18-64 years)	3
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with relapsed or refractory T-cell acute lymphoblastic leukemia (T-ALL) or T-cell lymphoblastic lymphoma (T-LBL), who had adequate function of major organ systems and Eastern Cooperative Oncology Group scale of Performance Status (ECOG-PS) score ≤ 2 were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Adult
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Arm description:

Adult participants received nelarabine 1000 milligrams (mg)/square meter (m^2) in the first cycle and nelarabine 1500 mg/ m^2 in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of adult participants received nelarabine 1500 mg/ m^2 through all treatment cycles.

Arm type	Experimental
Investigational medicinal product name	Nelarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Nelarabine infusion 1000 milligrams (mg)/square meter (m^2) or 1500 mg/ m^2 for adult participants and 400 mg/ m^2 or 650 mg/ m^2 for pediatric participants

Arm title	Pediatric (Cohorts 1 and 2)
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Arm description:

Pediatric participants received nelarabine 400 mg/ m^2 in the first cycle and nelarabine 650 mg/ m^2 in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of pediatric participants received nelarabine 650 mg/ m^2 through all treatment cycles.

Arm type	Experimental
Investigational medicinal product name	Nelarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Nelarabine infusion 1000 milligrams (mg)/square meter (m^2) or 1500 mg/ m^2 for adult participants and 400 mg/ m^2 or 650 mg/ m^2 for pediatric participants

Arm title	Pediatric (Cohort 3)
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Arm description:

Pediatric participants received nelarabine 650 mg/ m^2 through all treatment cycles.

Arm type	Experimental
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Investigational medicinal product name	Nelarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Nelarabine infusion 1000 milligrams (mg)/square meter (m²) or 1500 mg/m² for adult participants and 400 mg/m² or 650 mg/m² for pediatric participants

Number of subjects in period 1	Adult	Pediatric (Cohorts 1 and 2)	Pediatric (Cohort 3)
Started	7	4	2
Completed	2	0	0
Not completed	5	4	2
Other reason	3	2	2
Lack of efficacy	2	2	-

Baseline characteristics

Reporting groups

Reporting group title	Adult
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Reporting group description:

Adult participants received nelarabine 1000 milligrams (mg)/square meter (m²) in the first cycle and nelarabine 1500 mg/m² in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of adult participants received nelarabine 1500 mg/m² through all treatment cycles.

Reporting group title	Pediatric (Cohorts 1 and 2)
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Reporting group description:

Pediatric participants received nelarabine 400 mg/m² in the first cycle and nelarabine 650 mg/m² in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of pediatric participants received nelarabine 650 mg/m² through all treatment cycles.

Reporting group title	Pediatric (Cohort 3)
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Reporting group description:

Pediatric participants received nelarabine 650 mg/m² through all treatment cycles.

Reporting group values	Adult	Pediatric (Cohorts 1 and 2)	Pediatric (Cohort 3)
Number of subjects	7	4	2
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	24.1 ± 12.58	6.3 ± 3.77	9.5 ± 3.54
Gender categorical Units:			
Female	1	1	0
Male	6	3	2
Race, Customized Units: Subjects			
Asian-Japanese	7	4	2

Reporting group values	Total		
Number of subjects	13		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units:			
Female	2		
Male	11		

Race, Customized			
Units: Subjects			
Asian-Japanese	13		

End points

End points reporting groups

Reporting group title	Adult
Reporting group description: Adult participants received nelarabine 1000 milligrams (mg)/square meter (m ²) in the first cycle and nelarabine 1500 mg/m ² in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of adult participants received nelarabine 1500 mg/m ² through all treatment cycles.	
Reporting group title	Pediatric (Cohorts 1 and 2)
Reporting group description: Pediatric participants received nelarabine 400 mg/m ² in the first cycle and nelarabine 650 mg/m ² in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of pediatric participants received nelarabine 650 mg/m ² through all treatment cycles.	
Reporting group title	Pediatric (Cohort 3)
Reporting group description: Pediatric participants received nelarabine 650 mg/m ² through all treatment cycles.	
Subject analysis set title	Adult 1000 mg/m ²
Subject analysis set type	Sub-group analysis
Subject analysis set description: Adult participants who received nelarabine 1000 mg/m ² in the study	
Subject analysis set title	Adult 1500 mg/m ²
Subject analysis set type	Sub-group analysis
Subject analysis set description: Adult participants who received nelarabine 1500 mg/m ² in the study	

Primary: Best overall response with bone marrow involvement

End point title	Best overall response with bone marrow involvement ^{[1][2]}
End point description: The best overall response was assessed from the overall response (Complete Response (CR), CR with/without hematologic recovery (CR*), Partial Response (PR), and treatment failure) throughout the study. Efficacy Population: all participants with evaluable efficacy data at screening and at least one post-dose assessment time (that is, who are evaluable for disease state). Only participants with available data were analyzed.	
End point type	Primary
End point timeframe: Up to approximately 5 months	

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: There are no statistical data to report.

[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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Adult	Pediatric (Cohorts 1 and 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4 ^[3]	4		
Units: Participants				
CR	1	2		
CR*	0	0		
PR	0	0		

Treatment failure	2	2		
Missing	1	0		

Notes:

[3] - Efficacy Population

Statistical analyses

No statistical analyses for this end point

Primary: Best overall response without bone marrow involvement

End point title	Best overall response without bone marrow involvement ^{[4][5]}
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End point description:

The best overall response was assessed from the overall response (Complete Response (CR), Partial Response (PR), Stable Disease (SD), and Progressive Disease (PD)) throughout the study. Efficacy Population: all participants with evaluable efficacy data at screening and at least one post-dose assessment time (that is, who are evaluable for disease state). Only participants with available data were analyzed.

End point type	Primary
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End point timeframe:

Up to approximately 5 months

Notes:

[4] - 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: There are no statistical data to report.

[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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Adult	Pediatric (Cohorts 1 and 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3 ^[6]	0 ^[7]		
Units: Participants				
CR	0			
PR	0			
SD	2			
PD	1			

Notes:

[6] - Efficacy Population

[7] - Participants were not analyzed as data were not available.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with response with bone marrow involvement

End point title	Number of participants with response with bone marrow involvement ^{[8][9]}
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End point description:

Response is defined as participants with CR, CR*, or PR. Only participants with available data were analyzed.

End point type	Primary
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End point timeframe:

Up to approximately 5 months

Notes:

[8] - 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: There are no statistical data to report.

[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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Adult	Pediatric (Cohorts 1 and 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4 ^[10]	4		
Units: Participants	1	2		

Notes:

[10] - Efficacy Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with response without bone marrow involvement

End point title	Number of Participants with response without bone marrow involvement ^{[11][12]}
End point description: Response is defined as number of participants with CR or PR. Only participants with available data were analyzed.	
End point type	Primary
End point timeframe: Up to approximately 5 months	

Notes:

[11] - 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: There are no statistical data to report.

[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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Adult	Pediatric (Cohorts 1 and 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3 ^[13]	0 ^[14]		
Units: Participants	0			

Notes:

[13] - Efficacy Population

[14] - Participants were not analyzed as data were not available.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with response with or without bone marrow involvement

End point title	Number of participants with response with or without bone marrow involvement ^{[15][16]}
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End point description:

Response is defined as number of participants with CR, CR*, or PR.

End point type	Primary
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End point timeframe:

Up to approximately 5 months

Notes:

[15] - 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: There are no statistical data to report.

[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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Adult	Pediatric (Cohorts 1 and 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[17]	4		
Units: Participants	1	2		

Notes:

[17] - Efficacy Population

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) parameters of plasma nelarabine: area under the plasma concentration-time curve (AUC) from time zero to the last measurable concentration (AUC0-t) and AUC from time zero to infinity (AUC0-infinity)

End point title	Pharmacokinetic (PK) parameters of plasma nelarabine: area under the plasma concentration-time curve (AUC) from time zero to the last measurable concentration (AUC0-t) and AUC from time zero to infinity (AUC0-infinity) ^[18]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the nelarabine concentrations were assessed in plasma. Nelarabine PK parameters were derived by PK analysis using nelarabine concentrations. PK Population: all participants with evaluable PK data.

End point type	Primary
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End point timeframe:

Pre-dose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[18] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[19]	6		
Units: hour*micromole per liter				
geometric mean (confidence interval 95%)				
AUC0-t	36.09 (8.34 to 156.14)	32.75 (17.35 to 61.83)		
AUC0-infinity	36.27 (8.44 to 155.83)	32.97 (17.5 to 62.12)		

Notes:

[19] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma nelarabine: maximum observed plasma concentration (Cmax)

End point title	PK parameters of plasma nelarabine: maximum observed plasma concentration (Cmax) ^[20]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the nelarabine concentrations were assessed in plasma. Nelarabine PK parameters were derived by PK analysis using nelarabine concentrations.

End point type	Primary
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End point timeframe:

Pre-dose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[20] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[21]	6		
Units: micromole per liter				
geometric mean (confidence interval 95%)	28.3229 (6.8186 to 117.6465)	26.2848 (14.1822 to 48.7152)		

Notes:

[21] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma nelarabine: time for Cmax (tmax)

End point title	PK parameters of plasma nelarabine: time for Cmax (tmax) ^[22]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the nelarabine concentrations were assessed in plasma. Nelarabine PK parameters were derived by PK analysis using

nelarabine concentrations.

End point type	Primary
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End point timeframe:

Pre-dose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[22] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[23]	6		
Units: hours				
median (full range (min-max))	2 (2 to 2)	2.04 (2 to 2.2)		

Notes:

[23] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma nelarabine: half-life (t_{1/2})

End point title	PK parameters of plasma nelarabine: half-life (t _{1/2}) ^[24]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the nelarabine concentrations were assessed in plasma. Nelarabine PK parameters were derived by PK analysis using nelarabine concentrations.

End point type	Primary
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End point timeframe:

Pre-dose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[24] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[25]	6		
Units: hours				
geometric mean (confidence interval 95%)	0.3043 (0.1579 to 0.5865)	0.2324 (0.1607 to 0.3361)		

Notes:

[25] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma nelarabine: clearance (CL)

End point title	PK parameters of plasma nelarabine: clearance (CL) ^[26]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the nelarabine concentrations were assessed in plasma. Nelarabine PK parameters were derived by PK analysis using nelarabine concentrations.

End point type	Primary
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End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[26] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[27]	6		
Units: Liters per hour				
geometric mean (confidence interval 95%)	148.26 (37.75 to 582.36)	243.99 (133.57 to 445.7)		

Notes:

[27] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma nelarabine: steady state volume of distribution (V_{ss})

End point title	PK parameters of plasma nelarabine: steady state volume of distribution (V _{ss}) ^[28]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the nelarabine concentrations were assessed in plasma. Nelarabine PK parameters were derived by PK analysis using nelarabine concentrations.

End point type	Primary
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End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[28] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[29]	6		
Units: Liters				
geometric mean (confidence interval 95%)	65.08 (30.73 to 137.85)	81.8 (57.19 to 116.99)		

Notes:

[29] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma 9-beta-D-arabinofuranosyl guanine (ara-G): AUC0-t and AUC0-infinity

End point title	PK parameters of plasma 9-beta-D-arabinofuranosyl guanine (ara-G): AUC0-t and AUC0-infinity ^[30]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the ara-G concentrations were assessed in plasma. PK parameters for ara-G were derived by PK analysis using ara-G concentrations.

End point type	Primary
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End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[30] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[31]	6		
Units: hour*micromole per liter				
geometric mean (confidence interval 95%)				
AUC0-t	436.96 (259.24 to 736.53)	616.42 (389.17 to 976.36)		
AUC0-infinity	440.73 (263 to 738.56)	622.54 (390.78 to 991.76)		

Notes:

[31] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma ara-G: Cmax

End point title	PK parameters of plasma ara-G: Cmax ^[32]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the ara-G concentrations were assessed in plasma. PK parameters for ara-G were derived by PK analysis using ara-G concentrations.

End point type	Primary
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End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[32] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[33]	6		
Units: micromole per liter				
geometric mean (confidence interval 95%)	86.9682 (65.1873 to 116.0267)	131.7519 (108.5299 to 159.9427)		

Notes:

[33] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma ara-G: tmax

End point title | PK parameters of plasma ara-G: tmax^[34]

End point description:

Blood samples were collected during the specified time points on Day 1 and the ara-G concentrations were assessed in plasma. PK parameters for ara-G were derived by PK analysis using ara-G concentrations.

End point type | Primary

End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[34] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[35]	6		
Units: hours				
median (full range (min-max))	2 (2 to 2)	2.105 (2 to 2.25)		

Notes:

[35] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma ara-G: half-life (t1/2)

End point title | PK parameters of plasma ara-G: half-life (t1/2)^[36]

End point description:

Blood samples were collected during the specified time points on Day 1 and the ara-G concentrations were assessed in plasma. PK parameters for ara-G were derived by PK analysis using ara-G concentrations.

End point type Primary

End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[36] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[37]	6		
Units: hours				
geometric mean (confidence interval 95%)	3.5417 (2.8113 to 4.4619)	2.9758 (2.1055 to 4.2059)		

Notes:

[37] - PK population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma ara-G: apparent total clearance (CL/F)

End point title PK parameters of plasma ara-G: apparent total clearance (CL/F)^[38]

End point description:

Blood samples were collected during the specified time points on Day 1 and the ara-G concentrations were assessed in plasma. PK parameters for ara-G were derived by PK analysis using ara-G concentrations.

End point type Primary

End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[38] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[39]	6		
Units: Liters per hour				
geometric mean (confidence interval 95%)	12.2 (7.72 to 19.3)	12.92 (8.23 to 20.29)		

Notes:

[39] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters of plasma ara-G: steady state apparent volume of distribution (Vss/F)

End point title	PK parameters of plasma ara-G: steady state apparent volume of distribution (Vss/F) ^[40]
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End point description:

Blood samples were collected during the specified time points on Day 1 and the ara-G concentrations were assessed in plasma. PK parameters for ara-G were derived by PK analysis using ara-G concentrations.

End point type	Primary
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End point timeframe:

Predose, and 0.0, 0.25, 0.5, 1, 2, 3, 5, 7, 10, and 22 hours post-dose on Day 1 and Day 5 (22 hours post-dose on Day 5 was optional)

Notes:

[40] - 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: There are no statistical data to report.

End point values	Adult 1000 mg/m ²	Adult 1500 mg/m ²		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 ^[41]	6		
Units: Liters				
geometric mean (confidence interval 95%)	62.35 (31.32 to 124.15)	55.48 (41.92 to 73.44)		

Notes:

[41] - PK Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were assessed from Baseline to end of study (approximately 2.5 months).

Adverse event reporting additional description:

SAEs and non-serious AEs were analyzed in Safety Population, which was defined as all participants who received at least one dose of study medication. Non-serious AEs are presented for if they occurred in more than one patient in any treatment. The # of occurrences information is not available; therefore, the # of occurrences = # participants.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.1
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Reporting groups

Reporting group title	Adult
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Reporting group description:

Adult participants received nelarabine 1000 milligrams (mg)/square meter (m²) in the first cycle and nelarabine 1500 mg/m² in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of adult participants received nelarabine 1500 mg/m² through all treatment cycles.

Reporting group title	Pediatric (Cohorts 1 and 2)
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Reporting group description:

Pediatric participants received nelarabine 400 mg/m² in the first cycle and nelarabine 650 mg/m² in the second cycle and subsequent cycles in Cohort 1. Another group (Cohort 2) of pediatric participants received nelarabine 650 mg/m² through all treatment cycles.

Reporting group title	Pediatric (Cohort 3)
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Reporting group description:

Pediatric participants received nelarabine 650 mg/m² through all treatment cycles.

Serious adverse events	Adult	Pediatric (Cohorts 1 and 2)	Pediatric (Cohort 3)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Herpes zoster			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 2 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adult	Pediatric (Cohorts 1 and 2)	Pediatric (Cohort 3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	2 / 2 (100.00%)
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	4 / 7 (57.14%)	3 / 4 (75.00%)	1 / 2 (50.00%)
occurrences (all)	4	3	1
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 7 (57.14%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Alanine aminotransferase increased			
subjects affected / exposed	4 / 7 (57.14%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
White blood cell count decreased			
subjects affected / exposed	3 / 7 (42.86%)	3 / 4 (75.00%)	2 / 2 (100.00%)
occurrences (all)	3	3	2
Haemoglobin decreased			
subjects affected / exposed	2 / 7 (28.57%)	3 / 4 (75.00%)	0 / 2 (0.00%)
occurrences (all)	2	3	0
Blood urine present			
subjects affected / exposed	2 / 7 (28.57%)	3 / 4 (75.00%)	0 / 2 (0.00%)
occurrences (all)	2	3	0
Neutrophil count decreased			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	1 / 2 (50.00%)
occurrences (all)	2	2	1
Platelet count decreased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Urobilin urine present			

subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Nervous system disorders			
Somnolence			
subjects affected / exposed occurrences (all)	7 / 7 (100.00%) 7	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Headache			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Malaise			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed occurrences (all)	5 / 7 (71.43%) 5	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Abdominal pain			
subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Diarrhoea			
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 4 (50.00%) 2	0 / 2 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Rash			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 4 (50.00%) 2	0 / 2 (0.00%) 0
Infections and infestations			
Gingival swelling subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 4 (0.00%) 0	0 / 2 (0.00%) 0

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