Clinical trial results:
A Phase I/II open-label, single-arm, multi-center study of ruxolitinib added to corticosteroids in pediatric subjects with Grade II-IV acute graft vs. host disease after allogeneic hematopoietic stem cell transplantation.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Summary

EudraCT number	2018-000422-55
Trial protocol	SI BE FR DE ES NL IT DK CZ
Global end of trial date	02 February 2023
Results information	
Result version number	v1 (current)
This version publication date	18 August 2023
First version publication date	18 August 2023

Trial information

Trial identification	
Sponsor protocol code	CINC424F12201
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03491215
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novatis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novatis.email@novartis.com

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000901-PIP03-16

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	02 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I:
To assess pharmacokinetic (PK) parameters of ruxolitinib for subjects with acute GvHD and SR-acute GvHD and define an age appropriate RP2D for each of the groups 2-4.
.Group 2: age = 6 to < 12 years
.Group 3: age = 2 to < 6 years
.Group 4: age = 28 days to < 2 years

Phase II:
To measure the activity of ruxolitinib in subjects with acute GvHD or SR-acute GvHD assessed by Overall Response Rate (ORR) at Day 28.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Spain: 8

Worldwide total number of subjects	45
EEA total number of subjects	33

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)	27
Adolescents (12-17 years)	18
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

45 subjects enrolled in the study & treated with the confirmed RP2D; at least 20% had treatment naïve acute GvHD & at least 40% had SR-acute GvHD. Single arm study with subjects grouped as follows: Group 1: subjects ≥ 12y to < 18y, Group 2: subjects ≥ 6y to < 12y, Group 3: subjects ≥ 2y to < 6y, Group 4 was to include subjects ≥ 28 days to < 2y.

Pre-assignment

Screening details:

Five subjects were to be enrolled to each age group with no minimum for Group 4. The study was conducted in 8 countries and 19 centers.

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	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID

Arm description:

All patients received ruxolitinib (RUX) 10 mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ruxolitinib 10 mg BID

Arm title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID

Arm description:

All patients received RUX 5mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Ruxolitinib 5 mg hard non-gelatin capsule formulation

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ruxolitinib 5 mg BID

Arm title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID

Arm description:	
All patients received RUX 4mg/m^2 BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use
Dosage and administration details:	
Ruxolitinib 4mg/m2 BID	
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use
Dosage and administration details:	
Ruxolitinib 4mg/m2 BID	

Number of subjects in period 1	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID
Started	18	12	15
Completed	11	10	14
Not completed	7	2	1
Adverse event, serious fatal	6	2	1
Physician decision	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID
Reporting group description:	
All patients received ruxolitinib (RUX) 10 mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Reporting group title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID
Reporting group description:	
All patients received RUX 5mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Reporting group title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID
Reporting group description:	
All patients received RUX 4mg/m^2 BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)	

Reporting group values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID
Number of subjects	18	12	15
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	12	15
Adolescents (12-17 years)	18	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Months			
arithmetic mean	172.7	86.1	45.5
standard deviation	± 18.94	± 11.08	± 14.57
Sex: Female, Male Units: Participants			
Female	5	7	5
Male	13	5	10
Race/Ethnicity, Customized Units: Subjects			
White	11	5	4
Asian	3	3	5
Missing -Note: race is not collected in France	4	4	6

Reporting group values	Total		
Number of subjects	45		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	27		
Adolescents (12-17 years)	18		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: Months			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	17		
Male	28		
Race/Ethnicity, Customized			
Units: Subjects			
White	20		
Asian	11		
Missing -Note: race is not collected in France	14		

Subject analysis sets

Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID capsule in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID liquid in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)	
Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor	

(CNI)

Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received RUX 4mg/m^2 BID liquid in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received RUX 5mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)

Subject analysis set title	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) 10 mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All Subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All Subjects (Group 1, Group 2, & Group 3)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	Group 1: ≥ 12y to < 18y - RUX 10mg BID
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) 10 mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	Overall Response Rate (ORR) at Day 28 (>=2y-<6y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed

response or non-response. This assessment is for participants in group 3.

Subject analysis set title	ORR at Day 28 (>=6y-<12y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. This assessment is for participants in group 2.

Subject analysis set title	ORR at Day 28 (>=12y-<18y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. This assessment is for participants in group 1.

Subject analysis set title	Durable response rate (DRR) at Day 56 (>=2-<12)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

DRR at Day 56 was defined as the percentage of all subjects who achieved a complete response (CR) or partial response (PR) at Day 28 and maintained a CR or PR at Day 56. This assessment was for participants from age 12 years and above.

Subject analysis set title	AUClast Day 1: 1st quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	AUClast Day 1: 2nd quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	AUClast Day 1: 3rd quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	AUClast Day 1: 4th quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)

Subject analysis set title	Bleeding (>=2y-<6y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one bleeding event in group 3.

Subject analysis set title	Bleeding (>=6y-<12y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one bleeding event in group 2.

Subject analysis set title	Bleeding (>=12y-<18y
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one bleeding event in group 1.

Subject analysis set title	Infection (>=2y-<6y
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one infection in group 3.

Subject analysis set title	Infection (>=6y-<12y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one infection in group 2.

Subject analysis set title	Infection (>=12y-<18y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one infection in group 1.

Reporting group values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Number of subjects	2	8	8
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months			
arithmetic mean	154	259	372
standard deviation	± 58.1	± 53.6	± 58.6
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Number of subjects	7	5	5
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	 239 ± 65.3	 1.66 ± 17.5	 1.86 ± 29.9
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Number of subjects	5	7	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	 1.78 ± 66.3	 9.07 ± 214.0	 6.18 ± 195.8
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	All subjects (Group 1, Group 2 & Group 3)	All Subjects (Group 1, Group 2 & Group 3)
Number of subjects	18	38	45
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Months			
arithmetic mean	83.3		
standard deviation	±	±	±
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
White			
Asian			
Missing -Note: race is not collected in France			

Reporting group values	All Subjects (Group 1, Group 2, & Group 3)	All subjects (Group 1, Group 2 & Group 3)	All subjects (Group 1, Group 2 & Group 3)
Number of subjects	45	27	45
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Months			
arithmetic mean			
standard deviation	±	±	±

Sex: Female, Male Units: Participants			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
White			
Asian			
Missing -Note: race is not collected in France			

Reporting group values	Group 1: ≥ 12y to < 18y - RUX 10mg BID	Overall Response Rate (ORR) at Day 28 (>=2y-<6y)	ORR at Day 28 (>=6y-<12y)
Number of subjects	18	15	11
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous Units: Months			
arithmetic mean	0.0	13	10
standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
White			
Asian			
Missing -Note: race is not collected in France			

Reporting group values	ORR at Day 28 (>=12y-<18y)	Durable response rate (DRR) at Day 56 (>=2-<12)	AUClast Day 1: 1st quartile
Number of subjects	19	23	7
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			

Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	 17 ±	 20 ±	 ±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	AUClast Day 1: 2nd quartile	AUClast Day 1: 3rd quartile	AUClast Day 1: 4th quartile
Number of subjects	8	7	8
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	 ±	 ±	 ±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Bleeding (>=2y-<6y)	Bleeding (>=6y-<12y)

	capsule		
Number of subjects	15	15	11
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	Bleeding (>=12y-<18y	Infection (>=2y-<6y	Infection (>=6y-<12y)
Number of subjects	19	15	11
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female			

Male			

Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

Reporting group values	Infection (>=12y-<18y)		
Number of subjects	19		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Months arithmetic mean standard deviation	±		
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
White Asian Missing -Note: race is not collected in France			

End points

End points reporting groups

Reporting group title	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID
Reporting group description:	
All patients received ruxolitinib (RUX) 10 mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Reporting group title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID
Reporting group description:	
All patients received RUX 5mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Reporting group title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID
Reporting group description:	
All patients received RUX 4mg/m^2 BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID capsule in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID liquid in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)	
Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 4mg/m^2 BID liquid in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients received RUX 5mg BID tablet in addition to corticosteroids +/-calcineurin inhibitor (CNI)	
Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)

Subject analysis set title	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) 10 mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All Subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All Subjects (Group 1, Group 2, & Group 3)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	All subjects (Group 1, Group 2 & Group 3)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) regardless of dose and age group, in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	Group 1: ≥ 12y to < 18y - RUX 10mg BID
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received ruxolitinib (RUX) 10 mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Subject analysis set title	Overall Response Rate (ORR) at Day 28 (>=2y-<6y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. This assessment is for participants in group 3.

Subject analysis set title	ORR at Day 28 (>=6y-<12y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. This assessment is for participants in group 2.

Subject analysis set title	ORR at Day 28 (>=12y-<18y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. This assessment is for participants in group 1.

Subject analysis set title	Durable response rate (DRR) at Day 56 (>=2-<12)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

DRR at Day 56 was defined as the percentage of all subjects who achieved a complete response (CR) or partial response (PR) at Day 28 and maintained a CR or PR at Day 56. This assessment was for participants from age 12 years and above.

Subject analysis set title	AUClast Day 1: 1st quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	AUClast Day 1: 2nd quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	AUClast Day 1: 3rd quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	AUClast Day 1: 4th quartile
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

Subject analysis set title	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients received RUX 4mg/m^2 BID capsule in addition to corticosteroids +/- calcineurin inhibitor (CNI)

Subject analysis set title	Bleeding (>=2y-<6y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one bleeding event in group 3.

Subject analysis set title	Bleeding (>=6y-<12y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one bleeding event in group 2.

Subject analysis set title	Bleeding (>=12y-<18y
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one bleeding event in group 1.

Subject analysis set title	Infection (>=2y-<6y
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one infection in group 3.

Subject analysis set title	Infection (>=6y-<12y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one infection in group 2.

Subject analysis set title	Infection (>=12y-<18y)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

These are the participants who had at least one infection in group 1.

Primary: Phase I: Measurement of pharmacokinetic (PK) parameter, AUClast, in aGvHD and SR-aGvHD patients

End point title	Phase I: Measurement of pharmacokinetic (PK) parameter, AUClast, in aGvHD and SR-aGvHD patients[1]

End point description:

Measurement in acute GvHD and SR-acute GvHD subjects used extensive PK sampling in Groups 1-3 and sparse sampling in Group 4.
AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

End point type	Primary

End point timeframe:

Day 1

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	8	8
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	252 (± 186.6)	154 (± 58.1)	259 (± 53.6)	372 (± 58.6)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	239 (± 65.3)			

Statistical analyses

Statistical analysis title	Group 3 vs Group 2

Statistical analysis description:

Group 3 vs Group 2

Comparison groups	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.801
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.49
upper limit	1.311

Statistical analysis title	Group 2 vs. Group 1
Statistical analysis description:	
Group 2 vs. Group 1	
Comparison groups	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	1.237
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.639
upper limit	2.394

Statistical analysis title	Group 3 vs. Group 1
Statistical analysis description:	
Group 3 vs. Group 1	
Comparison groups	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.991
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.532
upper limit	1.846

Primary: Phase I: Measurement of PK parameter, Cmax, in aGvHD and SR-aGvHD patients

End point title	Phase I: Measurement of PK parameter, Cmax, in aGvHD and SR-aGvHD patients[2]

End point description:

Measurement in acute GvHD and SR-acute GvHD subjects used extensive PK sampling in Groups 1-3 and sparse sampling in Group 4.
Cmax: The maximum (peak) observed plasma drug concentration

End point type	Primary

End point timeframe:

Day 1

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	8	8
Units: ng/ML				
geometric mean (geometric coefficient of variation)	66.1 (± 169.8)	49.4 (± 45.7)	66.5 (± 60.8)	105 (± 71.4)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng/ML				
geometric mean (geometric coefficient of variation)	61.2 (± 81.1)			

Statistical analyses

Statistical analysis title	Group 3 vs. Group 2

Statistical analysis description:

Group 3 vs. Group 2

Comparison groups	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.709
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.425
upper limit	1.184

Statistical analysis title	Group 3 vs. Group 1
Statistical analysis description: Group 3 vs. Group 1	
Comparison groups	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.968
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.506
upper limit	1.851

Statistical analysis title	Group 2 vs. Group 1
Statistical analysis description: Group 2 vs. Group 1	
Comparison groups	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	1.365
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.686
upper limit	2.714

Primary: Phase I: Measurement of PK parameter, Ctrough, in aGvHD and SR-aGvHD patients

End point title	Phase I: Measurement of PK parameter, Ctrough, in aGvHD and SR-aGvHD patients[3]

End point description:

Measurement in acute GvHD and SR-acute GvHD subjects used extensive PK sampling in Groups 1-3 and sparse sampling in Group 4. Ctrough: The minimum observed plasma concentration at the end of an administration interval
(corresponding to the pre-dose concentration prior to the following administration).

End point type	Primary

End point timeframe:

Day 7

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	2	8	7
Units: ng/ml				
geometric mean (geometric coefficient of variation)	8.85 (± 538.6)	1.71 (± 1.2)	3.99 (± 277.1)	9.07 (± 214.0)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	6.18 (± 195.8)			

Statistical analyses

Statistical analysis title	Group 3 vs. Group 2

Statistical analysis description:

Group 3 vs. Group 2

Comparison groups	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.765
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.256
upper limit	2.28

Statistical analysis title	Group 2 vs. Group 1
Statistical analysis description:	
Group 2 vs. Group 1	
Comparison groups	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet v Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.707
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.178
upper limit	2.817

Statistical analysis title	Group 3 vs. Group 1
Statistical analysis description:	
Group 3 vs. Group 1	
Comparison groups	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule v Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.541
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.145
upper limit	2.023

Primary: Phase I: Measurement of PK parameter, T1/2, in aGvHD and SR-aGvHD patients

End point title	Phase I: Measurement of PK parameter, T1/2, in aGvHD and SR-aGvHD patients[4][5]

End point description:

Measurement in acute GvHD and SR-acute GvHD subjects used extensive PK sampling in Groups 1-3 and sparse sampling in Group 4.
T1/2: The elimination half-life associated with the terminal slope (Lambda_z) of a semi logarithmic concentration-time curve

End point type	Primary

End point timeframe:

Day 1

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: No statistical Analysis was planned.

[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: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	5	5
Units: ng/ml				
geometric mean (geometric coefficient of variation)	1.33 (± 31.7)	1.50 (± 6.5)	1.66 (± 17.5)	1.86 (± 29.9)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	1.78 (± 66.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase I: Age-based determination of recommended phase 2 dose (RP2D) for each of the groups 2 - 4 using AUClast

End point title	Phase I: Age-based determination of recommended phase 2 dose (RP2D) for each of the groups 2 - 4 using AUClast[6][7]

End point description:

Phase I: Age-based determination of RP2D was be based on observed PK parameters:

- Group 2: age ≥ 6 to < 12 years
- Group 3: age ≥ 2 to < 6 years
- Group 4: age = 28 days to < 2 years

The RP2D for Groups 2 and 3 was assessed for both activity and safety in Phase II, over a 24-week period.
AUClast: The AUC from time zero to the last measurable concentration sampling time (Tlast).

End point type	Primary

End point timeframe:

28 Days

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical Analysis was planned.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	8	8
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	252 (± 186.6)	154 (± 58.1)	259 (± 53.6)	372 (± 58.6)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	239 (± 65.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase I: Age-based determination of recommended phase 2 dose (RP2D) for each of the groups 2 - 4 using Cmax

End point title	Phase I: Age-based determination of recommended phase 2 dose (RP2D) for each of the groups 2 - 4 using Cmax[8][9]

End point description:

Phase I: Age-based determination of RP2D was be based on observed PK parameters:
- Group 2: age ≥ 6 to < 12 years
- Group 3: age ≥ 2 to < 6 years
- Group 4: age = 28 days to < 2 years

The RP2D for Groups 2 and 3 was assessed for both activity and safety in Phase II, over a 24-week period.

Cmax: The maximum (peak) observed plasma drug concentration.

End point type	Primary

End point timeframe:

28 Days

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: No statistical Analysis was planned.

[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: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	8	8
Units: ng/mL				
geometric mean (geometric coefficient of variation)	66.1 (± 169.8)	49.4 (± 45.7)	66.5 (± 60.8)	105 (± 71.4)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	61.2 (± 81.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase I: Age-based determination of recommended phase 2 dose (RP2D) for each of the groups 2 - 4 using Ctrough

End point title	Phase I: Age-based determination of recommended phase 2 dose (RP2D) for each of the groups 2 - 4 using Ctrough[10][11]

End point description:

Phase I: Age-based determination of RP2D was be based on observed PK parameters:
- Group 2: age ≥ 6 to < 12 years
- Group 3: age ≥ 2 to < 6 years
- Group 4: age = 28 days to < 2 years

The RP2D for Groups 2 and 3 was assessed for both activity and safety in Phase II, over a 24-week period.
Ctrough: The minimum observed plasma concentration at the end of an administration interval (corresponding to the pre-dose concentration prior to the following administration).

End point type	Primary

End point timeframe:

28 Days

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical Analysis was planned.

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID tablet
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	2	8	8
Units: ng/ml				
geometric mean (geometric coefficient of variation)	8.85 (± 538.6)	1.71 (± 1.2)	3.99 (± 277.1)	10.6 (± 208.1)

End point values	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	6.18 (± 195.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase II: Overall response rate (ORR)

End point title	Phase II: Overall response rate (ORR)[12][13]

End point description:

Phase II: ORR is defined as the percentage of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response. Scoring of response was relative to the organ stage at the start of the study treatment.

End point type	Primary

End point timeframe:

Day 28

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical Analysis was planned.

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	15	18	
Units: Percentage of participants				
number (confidence interval 90%)	83.3 (56.2 to 97.0)	86.7 (63.7 to 97.6)	83.3 (62.3 to 95.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of all patients who achieved a complete response (CR) or partial response (PR) (Durable Overall Response Rate (ORR))

End point title	Percentage of all patients who achieved a complete response (CR) or partial response (PR) (Durable Overall Response Rate (ORR))[14]

End point description:

Durable ORR at Day 56 was defined as the percentage of all subjects who achieved a complete response (CR) or partial response (PR) at Day 28 and maintained a CR or PR at Day 56.
Complete-response was defined as a score of 0 for the acute GvHD grading in all evaluable organs that indicates complete resolution of all signs and symptoms of acute GvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response or non-response of acute GvHD.
Partial response was defined as improvement of 1 stage in 1 or more organs involved with acute GvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response
or non-response of acute GvHD.

End point type	Secondary

End point timeframe:

Day 56

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	15	18	
Units: Percentage of participants				
number (confidence interval 90%)	75.0 (47.3 to 92.8)	73.3 (48.9 to 90.3)	55.6 (34.1 to 75.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients who achieved OR (CR+PR) at Day 14

End point title	Percentage of patients who achieved OR (CR+PR) at Day 14[15]

End point description:

ORR at Day 14 was defined as the proportion of subjects with CR or PR at Day 14 according to standard criteria.

End point type	Secondary

End point timeframe:

Day 14

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	15	18	
Units: Percentage of participants				
number (confidence interval 90%)	66.7 (39.1 to 87.7)	86.7 (63.7 to 97.6)	72.2 (50.2 to 88.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Area under the curve (AUClast) versus safety

End point title	PK parameter: Area under the curve (AUClast) versus safety

End point description:

To assess pharmacokinetic/pharmacodynamic relationship (comparison of AUClast with safety). This analysis includes subjects from both F12201 study (pediatrics) and C2301 study (adolescents+adults).

End point type	Secondary

End point timeframe:

24 weeks

End point values	Bleeding (>=2y-<6y)	Bleeding (>=6y-<12y)	Bleeding (>=12y-<18y	Infection (>=2y-<6y
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	11	19	15
Units: Rvent rate				
number (not applicable)	6.7	18.2	26.3	60

End point values	Infection (>=6y-<12y)	Infection (>=12y-<18y)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	19		
Units: Rvent rate				
number (not applicable)	63.6	52.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Weekly cumulative steroid dose for each patient up to Day 56

End point title	Weekly cumulative steroid dose for each patient up to Day

End point description:

The weekly cumulative steroid dose was calculated for each subject up to Day 56 and the overall cumulative steroid dose was calculated for each subject at Day 56.

End point type	Secondary

End point timeframe:

up to 56 days (Week 1 - Week 8)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	15	18	
Units: mg/kg				
arithmetic mean (standard deviation)				
Week 1	14.1 (± 4.60)	11.9 (± 5.32)	12.6 (± 6.04)	
Week 2	26.1 (± 9.91)	21.0 (± 8.03)	21.9 (± 10.79)	
Week 3 (n = 17, 12, 15)	36.5 (± 17.18)	29.0 (± 10.20)	30.1 (± 16.14)	
Week 4 (n= 16, 10, 14)	46.9 (± 24.91)	36.8 (± 12.95)	37.5 (± 21.19)	
Week 5 (n = 16, 10, 14)	55.2 (± 31.52)	42.0 (± 14.76)	42.6 (± 24.05)	
Week 6 (n =13, 10, 10)	61.8 (± 35.80)	48.8 (± 17.68)	48.9 (± 24.57)	
Week 7 (n = 11, 9, 10	60.6 (± 35.75)	53.7 (± 19.32)	51.5 (± 28.34)	
Weel 8 (n = 9, 7, 10)	73.6 (± 43.11)	58.1 (± 20.50)	61.3 (± 30.29)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

Duration of response was defined as the time from first response (PR or CR) until acute GvHD progression, or the date of additional systemic therapy for acute GvHD. Death without prior observation of acute GvHD progression, and onset of chronic GvHD are considered to be competing risks. Duration of response will be censored at the last response assessment prior to or at the analysis cut-off date, if no events/competing risks occurred on or before 4 weeks (28 days) after the last GvHD assessment. The estimated probability of loss of response at 1, 2 and 6 months after participant's first achievement of CR or PR has been reported.

End point type	Secondary

End point timeframe:

Months 1, 2 & 6

End point values	All subjects (Group 1, Group 2 & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	38			
Units: Probability of loss of response				
number (confidence interval 95%)				
1 Month	2.63 (0.20 to 11.98)			
2 Months	5.41 (0.95 to 16.13)			
6 Months	20.37 (8.74 to 35.40)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) per Kaplan Meier

End point title	Overall Survival (OS) per Kaplan Meier

End point description:

OS is defined as the time from the start of treatment to the date of death due to any cause. If a subject was not known to have died, then OS was censored at the latest date the subject was known to be alive. The estimated survival probability at 1,2,6,12,18 months after start of treatment has been reported. (on or before the cut-off date).

End point type	Secondary
End point timeframe: 1 Month (M), 2 M, 6M, 12M, 18M	

End point values	All Subjects (Group 1, Group 2 & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: survival probability				
number (confidence interval 95%)				
1 Month	100 (100 to 100)			
2 Months	100 (100 to 100)			
6 Months	93.33 (80.74 to 97.80)			
12 Months	88.83 (75.22 to 95.19)			
18 Months	79.72 (64.64 to 88.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS) per Kaplan-Meier estimates

End point title	Event-Free Survival (EFS) per Kaplan-Meier estimates
End point description: EFS is defined as the time from start of treatment to the date of hematologic disease relapse/progression, graft failure, or death due to any cause. If a subject was not known to have any event, then EFS was censored at the latest date the subject was known to be alive (on or before the cut-off date).The estimated probability of event free at 1,2,6,12,18 months after start of treatment has been reported.	
End point type	Secondary
End point timeframe: 1 Month (M), 2 M, 6M, 12M, 18M	

End point values	All Subjects (Group 1, Group 2 & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: probability of event free				
number (confidence interval 95%)				

1 Month	100 (100 to 100)			
2 Months	97.78 (88.25 to 99.68)			
6 Months	91.11 (78.03 to 96.57)			
12 Months	86.61 (72.59 to 93.75)			
18 Months	79.77 (64.72 to 88.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Non Relapse Mortality (NRM)

End point title	Non Relapse Mortality (NRM)

End point description:

NRM is defined as the time from start of treatment to date of death not preceded by hematologic disease relapse/progression. The estimated probability of non-relapse mortality at 1,2,6,12,16,24 months after start of treatment has been reported.

End point type	Secondary

End point timeframe:

Month (M) 1, M2, M6, M12, M18, M24

End point values	All Subjects (Group 1, Group 2 & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Probability of non-relapse mortality				
number (confidence interval 95%)				
1 Month	999 (999 to 999)			
2 Months	999 (999 to 999)			
6 Months	4.44 (0.79 to 13.47)			
12 Months	8.95 (2.81 to 19.58)			
18 Months	13.50 (5.40 to 25.31)			
24 Months	13.50 (5.40 to 25.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Failure-Free Survival (FFS)

End point title	Failure-Free Survival (FFS)

End point description:

Failure-free survival was defined as the time from start date of treatment to any of the following: hematologic relapse/progression, non-relapse mortality (NRM) or addition of new systemic acute GvHD treatment. The estimated probability of the onset of failure event at 1,2,6,12,18,24 months after start of treatment has been reported.

End point type	Secondary

End point timeframe:

1 Month (M), 2M, 6M, 12M, 18M, 24M

End point values	All Subjects (Group 1, Group 2, & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Prob. of the onset of failure event				
number (confidence interval 95%)				
1 Month	11.11 (4.02 to 22.27)			
2 Months	13.33 (5.34 to 25.01)			
6 Months	26.67 (14.72 to 40.18)			
12 Months	26.67 (14.72 to 40.18)			
18 Months	28.97 (16.48 to 42.68)			
24 Months	28.97 (16.48 to 42.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Malignancy Relapse/Progression (MR)

End point title	Incidence of Malignancy Relapse/Progression (MR)

End point description:

MR was defined as the time from start of treatment to hematologic malignancy relapse/progression. Calculated for patients with underlying hematologic malignant disease. The estimated probability of non-relapse mortality at 1,2,6,12,16,24 months after start of treatment has been reported.

End point type	Secondary

End point timeframe:

Month (M) 1, M2, M6, M12, M18, M24,

End point values	All subjects (Group 1, Group 2 & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Prob. of malignancy relapse/progression				
number (confidence interval 95%)				
Month 1	999 (999 to 999)			
Month 2	3.70 (0.25 to 16.23)			
Month 6	7.41 (1.24 to 21.37)			
12 Months	7.41 (1.24 to 21.37)			
18 Months	11.28 (2.74 to 26.60)			
Month 24	11.28 (2.74 to 26.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence of cGvHD

End point title	Cumulative Incidence of cGvHD

End point description:

cGvHD is defined as the diagnosis of any cGvHD including mild, moderate, severe. Incidence of chronic GvHD was the time from the start of treatment to onset of chronic GvHD. Cumulative incidence of chronic GvHD was estimated, accounting for deaths without prior onset of chronic GvHD and hematologic disease relapse/progression as the competing risks. The estimated probability of cGvHD at 1, 2, 6, 12, 18 and 24 months after start of treatment has been reported.

End point type	Secondary

End point timeframe:

Month (M) 1, M2, M6, M12, M18, M24

End point values	All subjects (Group 1, Group 2 & Group 3)			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Probability of the onset of cGvHD				
number (confidence interval 95%)				
1 Month	999 (999 to 999)			

2 Months	2.22 (0.17 to 10.29)			
6 Months	11.11 (4.01 to 22.29)			
12 Months	20.07 (9.80 to 32.94)			
18 Months	24.65 (13.11 to 38.09)			
24 Months	24.65 (13.11 to 38.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Graft Failure

End point title	Graft Failure[17]

End point description:

This was assessed by donor cell chimerism, defined as initial whole blood or marrow donor chimerism for those who had ≥5% donor cell chimerism at baseline. If donor cell chimerism declined to <5% on subsequent measurements, graft failure was declared.

End point type	Secondary

End point timeframe:

2 years

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Group 1: ≥ 12y to < 18y - RUX 10mg BID	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	15	18	
Units: Percentage of participants				
number (not applicable)	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Questionnaire on acceptability and palatability

End point title	Questionnaire on acceptability and palatability

End point description:

Responses from the acceptability and palatability of the study drug (only for subjects administered with oral pediatric formulation starting treatment Day 1) were evaluated from a questionnaire completed by subjects, with the help from parents or caregivers as needed at the following visits: Day 1 (after first dose), Week 4 (1 month) ((after either morning or evening dose of that visit date), Week 24 (6 months) (after either morning or evening dose of that visit date). The choices for taste of the medication were, 'Not good or bad', 'Very good or Good', or 'Bad'. The choices for aftertaste of the medication were, 'Not

good or bad' or 'Bad'. The choices for the smell of the medication were, 'Not good or bad' or 'Bad'.

End point type	Secondary

End point timeframe:

Day 1, Week 4 (1 month), Week 24 (6 months)

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID capsule	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID liquid	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	8	7	
Units: Responses from participants				
Day 1: Evaluator: Patient	0	1	0	
Day 1: Evaluator: Legal guardian	0	3	0	
Day 1: Evaluator: Parent	1	2	4	
Day 1: Evaluator: Caregiver	0	1	0	
Day 1: Evaluator: Health care professional	1	1	3	
Day 1: Taste of Medicine: Very good	0	3	0	
Day 1: Taste of Medicine: Good	1	2	0	
Day 1: Taste of Medicine: Not good or bad	1	0	3	
Day 1: Taste of Medicine: Bad	0	0	2	
Day 1: Taste of Med: Unable to answer question	0	3	2	
Day 1: Aftertaste of Medicine: Very good	0	1	0	
Day 1: Aftertaste of Medicine: Good	0	1	1	
Day 1: Aftertaste of Medicine: Not good or bad	2	1	3	
Day 1: Aftertaste of Medicine: Bad	0	0	2	
Day 1: Aftertaste of Medicine: Very bad	0	1	0	
Day1:Aftertaste of Med:Unable to answer question	0	4	1	
Day 1: Smell of Medicine: Very good	0	1	0	
Day 1: Smell of Medicine: Good	0	1	0	
Day 1: Smell of Medicine: Not good or bad	2	3	4	
Day 1: Smell of Medicine: Bad	0	0	1	
Day 1: Smell of Med: Unable to answer question	0	3	2	
Week 4: Evaluator: Legal guardian	0	2	1	
Week 4: Evaluator: Parent	1	4	5	
Week 4: Evaluator: Health care professional	1	2	0	
W4: Evaluator: NA as pt. disc. before assessment	0	0	1	
Week 4: Taste of Medicine: Good	2	4	1	
Week 4: Taste of Medicine: Not good or bad	0	1	4	
Week 4: Taste of Medicine: Very bad	0	0	1	
W4:Taste of Med: Unable to answer the question	0	3	0	

W4: Taste of Med: NA as pt. disc. before assess.	0	0	1	
Week 4: Aftertaste of Medicine: Good	0	2	1	
Week 4: Aftertaste of Medicine: Not good or bad	2	1	3	
Week 4: Aftertaste of Medicine: Bad	0	0	1	
W4: Aftertaste of Med:Unable to answer the quest	0	5	1	
Wk4:Aftertaste of Med:NA pt. disc b4 asses	0	0	1	
Week 4: Smell of Medicine: Very good	0	1	0	
Week 4: Smell of Medicine: Not good or bad	2	3	5	
Week 4: Smell of Medicine: Bad	0	1	0	
W4: Smell of Med: Unable to answer the quest.	0	3	1	
W4: Smell of Med: NA pt. disc. b4 asses.	0	0	1	
Week 24: Evaluator: Patient	0	1	1	
Week 24: Evaluator: Parent	0	0	1	
W24: Evaluator: Health care professional	0	1	0	
W24: Evaluator: NA as pt. disc. b4 assess	2	6	5	
Week 24: Taste of Medicine: Very good	0	2	0	
Week 24: Taste of Medicine: Good	0	0	1	
W24: Taste of Medicine: Not good or bad	0	0	1	
W24:Taste of Med: NA as pt. disc. before assess.	2	6	5	
Week 24: Aftertaste of Medicine: Very good	0	1	0	
W24: Aftertaste of Medicine: Not good or bad	0	0	2	
W24:Aftertaste of Med: Unable to answer question	0	1	0	
W24: Aftertaste of Med: NA as pt. disc. b4 asses.	2	6	5	
Week 24: Smell of Medicine: Very good	0	1	0	
Week 24: Smell of Medicine: Good	0	1	0	
Week 24: Smell of Medicine: Not good or bad	0	0	2	
W24: Smell of Med: NA as pt. disc. b4 asses.	2	6	5	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter - maximum serum concentration (Cmax) versus efficacy

End point title	PK parameter - maximum serum concentration (Cmax) versus efficacy[18]

End point description:

To assess pharmacokinetic/pharmacodynamic relationship (comparison of Cmax with efficacy). Cmax: The maximum (peak) observed plasma drug concentration.

End point type	Secondary

End point timeframe:

24 weeks

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID			
Subject group type	Reporting group			
Number of subjects analysed	0[19]			
Units: ng/ML				
geometric mean (geometric coefficient of variation)	()			

Notes:

[19] - The relationship between Cmax & efficacy was not investigated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Minimum serum concentration (Ctrough) versus safety

End point title	PK parameter: Minimum serum concentration (Ctrough) versus safety[20]

End point description:

To assess pharmacokinetic/pharmacodynamic relationships (comparison of Ctrough with safety).
Ctrough: The minimum observed plasma concentration at the end of an administration interval (corresponding to the pre-dose concentration prior to the following administration).

End point type	Secondary

End point timeframe:

24 weeks

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID			
Subject group type	Reporting group			
Number of subjects analysed	0[21]			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	()			

Notes:

[21] - The relationship between Ctrough & safety was not investigated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: AUClast versus efficacy

End point title	PK parameter: AUClast versus efficacy

End point description:

To assess the pharmacokinetic/pharmacodynamics relationship (comparison of AUClast with efficacy) by means of responders. This analysis includes subjects from both F12201 study (pediatrics) and C2301 study (adolescents + adults). Median taAUC was derived based on PopPK predicted time-averaged AUC0-12 until response.

End point type	Secondary

End point timeframe:

Day 28 (OR), Day 56 (DRR)

End point values	Overall Response Rate (ORR) at Day 28 (>=2y-<6y)	ORR at Day 28 (>=6y-<12y)	ORR at Day 28 (>=12y-<18y)	Durable response rate (DRR) at Day 56 (>=2-<12)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	11	19	23
Units: response rate				
number (not applicable)	86.7	90.9	89.5	87

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Cmax versus safety

End point title	PK parameter: Cmax versus safety[22]

End point description:

To assess pharmacokinetic/pharmacodynamics relationship (comparison of Cmax with safety). Cmax: The maximum (peak) observed plasma drug concentration.

End point type	Secondary

End point timeframe:

24 weeks

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID			
Subject group type	Reporting group			
Number of subjects analysed	0[23]			
Units: ng/ML				
geometric mean (geometric coefficient of variation)	()			

Notes:

[23] - The relationship between Cmax & safety was not investigated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Ctrough versus efficacy

End point title	PK parameter: Ctrough versus efficacy[24]

End point description:

To assess pharmacokinetic/pharmacodynamics relationship (comparison of Ctrough with efficacy). Ctrough: The minimum observed plasma concentration at the end of an administration interval (corresponding to the pre-dose concentration prior to the following administration).

End point type	Secondary

End point timeframe:

24 weeks

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID			
Subject group type	Reporting group			
Number of subjects analysed	0[25]			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	()			

Notes:

[25] - The relationship between Ctrough & efficacy was not investigated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: AUClast versus PD biomarkers

End point title	PK parameter: AUClast versus PD biomarkers

End point description:

Describe the relationship between AUC and PD biomarkers. This analysis includes subjects from both F12201 study (pediatrics) and C2301 study adolescents+adults). Population was divided by four level of exposure using AUClast Day 1 quartiles.

End point type	Secondary

End point timeframe:

Week 4

End point values	AUClast Day 1: 1st quartile	AUClast Day 1: 2nd quartile	AUClast Day 1: 3rd quartile	AUClast Day 1: 4th quartile
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	8	7	8
Units: Week 4 percentage change from baseline				
median (inter-quartile range (Q1-Q3))				
Biomarker: IL10	0.00 (-85.64 to 225.33)	-22.43 (-76.22 to 0.00)	-79.71 (-89.63 to -47.49)	-50.72 (-58.01 to 73.55)
Biomarker: IL6	-59.48 (-69.78 to 0.00)	-10.40 (-80.48 to 0.00)	0.00 (-67.78 to 0.00)	181.48 (0.00 to 376.54)
Biomarker: IL8	-63.63 (-70.48 to -21.03)	42.57 (-22.15 to 201.65)	31.79 (-48.56 to 329.67)	60.02 (-41.74 to 280.49)
Biomarker: TNFA	-61.45 (-74.05 to -56.96)	0.00 (-31.03 to 33.67)	-35.34 (-65.90 to -1.41)	21.49 (-48.52 to 311.76)
Biomarker: CD4 Assay (CD4 T cells) (%),	-40.49 (-42.67 to -35.51)	98.07 (16.40 to 206.34)	-3.07 (-17.66 to 115.79)	-42.67 (-62.47 to 92.71)
Biomarker: CD8 Assay (CD8 T cells) (%),	-51.80 (-69.95 to -20.07)	64.71 (6.18 to 118.32)	104.17 (-34.38 to 270.84)	33.77 (-76.27 to 114.61)
Biomarker: FOXP3 Assay (Treg cells) (%)	115.79 (-26.03 to 124.24)	43.15 (2.08 to 52.17)	57.14 (-16.49 to 79.73)	-11.11 (-60.56 to 119.05)
Biomarker: IL14A Assay (Th17 cells) (%)	5.33 (-33.75 to 10.78)	140.91 (-25.53 to 570.83)	-7.69 (-18.92 to 131.25)	38.73 (-57.47 to 203.45)
Biomarker: LRP5 Assay (B cells) (%),	-15.00 (-30.00 to 122.78)	25.78 (-42.86 to 300.00)	140.00 (37.80 to 142.86)	105.26 (-30.77 to 650.00)
MVD Assay (NK cells) (%)	-23.82 (-24.21 to 65.52)	61.81 (34.74 to 98.53)	22.54 (-18.99 to 69.08)	-0.71 (-34.19 to 72.62)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Cmax versus PD biomarkers

End point title	PK parameter: Cmax versus PD biomarkers[26]

End point description:

To assess pharmacokinetic/pharmacodynamic relationship (comparison of Cmax with PD biomarkers). Cmax: The maximum (peak) observed plasma drug concentration.

End point type	Secondary

End point timeframe:

24 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID			
Subject group type	Reporting group			
Number of subjects analysed	0[27]			
Units: ng/ML				
geometric mean (geometric coefficient of variation)	()			

Notes:

[27] - The relationship between Cmax & PD biomarker was not investigated.

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Ctrough versus PD biomarkers

End point title	PK parameter: Ctrough versus PD biomarkers[28]

End point description:

To assess pharmacokinetic/pharmacodynamics relationship (Ctrough with PD biomarkers). Ctrough: The minimum observed plasma concentration at the end of an administration interval (corresponding to the pre-dose concentration prior to the following administration).

End point type	Secondary

End point timeframe:

24 weeks

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID			
Subject group type	Reporting group			
Number of subjects analysed	0[29]			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	()			

Notes:

[29] - The relationship between Ctrough & PD biomarker was not investigated.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients who achieved Best Overall Response (BOR) up to Day 28

End point title	Percentage of patients who achieved Best Overall Response (BOR) up to Day 28[30]

End point description:

The best overall response (BOR) was defined as percentage of participants with (complete response (CR) or partial response (PR) at any time point and up to and including Day 28 and before the start of additional systemic therapy for acute GvHD (aGvHD).

End point type	Secondary

End point timeframe:

Up to 28 days and before start of additional aGvHD therapy

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID	Group 1: ≥ 12y to < 18y - RUX 10mg BID	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	15	18	
Units: Percentage of participants				
number (confidence interval 95%)	91.7 (66.1 to 99.6)	93.3 (83.7 to 98.2)	94.4 (76.2 to 99.7)	

Statistical analyses

No statistical analyses for this end point

Post-hoc: All Collected Deaths

End point title	All Collected Deaths[31]

End point description:

Adverse events and on-treatment deaths were collected from the first dose of study treatment up to 30 days after last dose of study medication, for a maximum duration of 380 days.

Post-treatment survival follow-up deaths were collected 31 days after last dose of study medication until the end of the study, up to approx. 23 months.

End point type	Post-hoc

End point timeframe:

AEs & On-treatment deaths: Up to approx. 380 days (13 months), Post-treatment survival follow-up deaths: Up to approx. 23 months after the end of treatment

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical Analysis was planned.

End point values	Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID capsule	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	18	15	
Units: Participants				
Total deaths	2	6	1	
On-treatment deaths	0	0	0	
Post-treatment deaths	2	6	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events and on-treatment deaths were collected from the first dose of study treatment up to 30 days after last dose of study medication, for a maximum duration of 380 days.

Adverse event reporting additional description:

Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Deaths in the post treatment survival follow-up are not considered Adverse Events. The total number at risk in the post treatment survival includes patients that entered the post treatment survival follow-up period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Arm: Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID

Reporting group description:

All patients received ruxolitinib (RUX) 10 mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Reporting group title	Arm: Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID

Reporting group description:

All patients received RUX 5mg BID in addition to corticosteroids +/-calcineurin inhibitor (CNI)

Reporting group title	Arm: Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID

Reporting group description:

All patients received RUX 4mg/m^2 BID in addition to corticosteroids +/-calcineurin inhibitor (CNI

Reporting group title	All Subjects

Reporting group description:

All Subjects from Group 1, Group 2 and Group 3 who were enrolled and participated in the study

Serious adverse events	Arm: Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Arm: Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Arm: Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 18 (61.11%)	7 / 12 (58.33%)	6 / 15 (40.00%)
number of deaths (all causes)	6	2	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Shock haemorrhagic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (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
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Pulmonary haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Investigations			
Adenovirus test positive			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Neutrophil count decreased			

subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Platelet count decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
White blood cell count decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus test positive			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Transplant dysfunction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (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
Nervous system disorders			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Immune thrombocytopenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Neutropenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Haemorrhagic disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Intestinal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Intestinal perforation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (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
Pancreatitis acute			

subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Acute kidney injury			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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			
COVID-19			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (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
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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

Sepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Viral haemorrhagic cystitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (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
Eye infection viral			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Herpes zoster			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Gastroenteritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hypokalaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (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
Acidosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 45 (53.33%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Vascular disorders			
Shock haemorrhagic			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage			

subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 1			
Pulmonary embolism				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract inflammation				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Adenovirus test positive				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus test positive				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				

Transplant dysfunction			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune thrombocytopenia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic disorder			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adenovirus infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Skin infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Viral haemorrhagic cystitis			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Device related infection			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye infection viral			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acidosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm: Group 1: subjects ≥ 12y to < 18y - RUX 10mg BID	Arm: Group 2: subjects ≥ 6y to < 12y - RUX 5mg BID	Arm: Group 3: subjects ≥ 2y to < 6y - RUX 4mg/m^2 BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)	12 / 12 (100.00%)	15 / 15 (100.00%)
Vascular disorders			
Microangiopathy			

subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Capillary leak syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	2 / 18 (11.11%)	2 / 12 (16.67%)	5 / 15 (33.33%)
occurrences (all)	2	2	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Catheter site erythema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 18 (11.11%)	2 / 12 (16.67%)	2 / 15 (13.33%)
occurrences (all)	4	5	2
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Acute graft versus host disease in intestine			

subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Allergy to immunoglobulin therapy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Drug hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Graft versus host disease in skin			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Penile erosion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bronchial disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	1 / 18 (5.56%)	2 / 12 (16.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Epistaxis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Productive cough			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pulmonary oedema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			

subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Investigations			
Adenovirus test positive			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	6 / 18 (33.33%)	2 / 12 (16.67%)	3 / 15 (20.00%)
occurrences (all)	6	2	3
Amylase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	3 / 15 (20.00%)
occurrences (all)	2	0	2
Blood bilirubin increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	2
Weight decreased			

subjects affected / exposed	0 / 18 (0.00%)	2 / 12 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus test positive			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	4 / 15 (26.67%)
occurrences (all)	1	2	8
Epstein-Barr virus test positive			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	2 / 12 (16.67%)	2 / 15 (13.33%)
occurrences (all)	2	3	5
Lipase increased			
subjects affected / exposed	2 / 18 (11.11%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 18 (5.56%)	2 / 12 (16.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	2
Neutrophil count decreased			
subjects affected / exposed	5 / 18 (27.78%)	2 / 12 (16.67%)	5 / 15 (33.33%)
occurrences (all)	12	3	18
Platelet count decreased			
subjects affected / exposed	0 / 18 (0.00%)	3 / 12 (25.00%)	6 / 15 (40.00%)
occurrences (all)	0	6	15
Prothrombin time abnormal			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Roseolovirus test positive			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Transaminases increased			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Weight increased			
subjects affected / exposed	1 / 18 (5.56%)	2 / 12 (16.67%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
White blood cell count decreased			
subjects affected / exposed	0 / 18 (0.00%)	2 / 12 (16.67%)	5 / 15 (33.33%)
occurrences (all)	0	2	8
Injury, poisoning and procedural complications			
Anaphylactic transfusion reaction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Post procedural contusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Post procedural haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Subcutaneous haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cardiac failure			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			

subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Post herpetic neuralgia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	6 / 18 (33.33%)	5 / 12 (41.67%)	10 / 15 (66.67%)
occurrences (all)	7	8	21
Febrile neutropenia			

subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Hyperleukocytosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	3 / 18 (16.67%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Lymphopenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	6 / 18 (33.33%)	0 / 12 (0.00%)	3 / 15 (20.00%)
occurrences (all)	6	0	3
Thrombotic microangiopathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	6 / 18 (33.33%)	2 / 12 (16.67%)	1 / 15 (6.67%)
occurrences (all)	10	4	3
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Eye disorder			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 18 (0.00%)	2 / 12 (16.67%)	3 / 15 (20.00%)
occurrences (all)	0	2	3
Angular cheilitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 18 (5.56%)	2 / 12 (16.67%)	2 / 15 (13.33%)
occurrences (all)	1	2	2
Diarrhoea			
subjects affected / exposed	3 / 18 (16.67%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	4	1	1
Intestinal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	2 / 15 (13.33%)
occurrences (all)	1	1	4
Anal fissure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Hypertransaminasaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Hirsutism			

subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Acne			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bullous haemorrhagic dermatosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 18 (0.00%)	2 / 12 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Ecchymosis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Eczema asteatotic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Night sweats			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Petechiae			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pruritus			

subjects affected / exposed	0 / 18 (0.00%)	2 / 12 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Purpura			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin striae			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	2 / 18 (11.11%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	2 / 18 (11.11%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Glycosuria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ketonuria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Micturition urgency			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Polyuria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	2 / 18 (11.11%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Renal impairment			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Urinary tract pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 18 (5.56%)	2 / 12 (16.67%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Cushingoid			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Amyotrophy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Muscle contracture			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Infections and infestations			

Atypical pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bacteraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
COVID-19			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Cystitis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Cytomegalovirus infection			
subjects affected / exposed	3 / 18 (16.67%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	4	0	0
Fungal infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	4
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Device related infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Ear infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Epstein-Barr virus infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Epstein-Barr virus infection reactivation			

subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	3 / 15 (20.00%)
occurrences (all)	0	1	3
Fungal foot infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus infection reactivation			
subjects affected / exposed	2 / 18 (11.11%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	3	1	1
Herpes simplex			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Klebsiella infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Mucosal infection			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Nail infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Otitis externa			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Rhinitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Staphylococcal sepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Varicella zoster virus infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Viraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Viral haemorrhagic cystitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vulvovaginitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Central obesity			
subjects affected / exposed	1 / 18 (5.56%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Decreased appetite			

subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Folate deficiency			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hyperferritinaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 12 (8.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 18 (11.11%)	3 / 12 (25.00%)	0 / 15 (0.00%)
occurrences (all)	4	5	0
Hypoglycaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 12 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	4 / 18 (22.22%)	3 / 12 (25.00%)	1 / 15 (6.67%)
occurrences (all)	4	3	0
Hypomagnesaemia			
subjects affected / exposed	2 / 18 (11.11%)	1 / 12 (8.33%)	1 / 15 (6.67%)
occurrences (all)	3	1	0
Hyperglycaemia			
subjects affected / exposed	3 / 18 (16.67%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 12 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	2	2
Metabolic acidosis			

subjects affected / exposed	1 / 18 (5.56%)	0 / 12 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 45 (100.00%)		
Vascular disorders			
Microangiopathy			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Capillary leak syndrome			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	9 / 45 (20.00%)		
occurrences (all)	9		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Catheter site erythema			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Face oedema			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pyrexia			

subjects affected / exposed occurrences (all)	6 / 45 (13.33%) 11		
Immune system disorders Hypogammaglobulinaemia subjects affected / exposed occurrences (all) Acute graft versus host disease in intestine subjects affected / exposed occurrences (all) Allergy to immunoglobulin therapy subjects affected / exposed occurrences (all) Drug hypersensitivity subjects affected / exposed occurrences (all) Graft versus host disease in skin subjects affected / exposed occurrences (all)	 2 / 45 (4.44%) 2 1 / 45 (2.22%) 2 1 / 45 (2.22%) 1 1 / 45 (2.22%) 1 1 / 45 (2.22%) 1		
Reproductive system and breast disorders Penile erosion subjects affected / exposed occurrences (all)	 1 / 45 (2.22%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Bronchial disorder subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	 1 / 45 (2.22%) 1 1 / 45 (2.22%) 1 4 / 45 (8.89%) 3 2 / 45 (4.44%) 3		

Productive cough			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pulmonary oedema			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Investigations			
Adenovirus test positive			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	11 / 45 (24.44%)		
occurrences (all)	11		
Amylase increased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	4		
Blood bilirubin increased			

subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Blood cholesterol increased				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences (all)	3			
Weight decreased				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences (all)	2			
C-reactive protein increased				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Cytomegalovirus test positive				
subjects affected / exposed	6 / 45 (13.33%)			
occurrences (all)	11			
Epstein-Barr virus test positive				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Gamma-glutamyltransferase increased				
subjects affected / exposed	5 / 45 (11.11%)			
occurrences (all)	10			
Lipase increased				
subjects affected / exposed	4 / 45 (8.89%)			
occurrences (all)	3			
Lymphocyte count decreased				
subjects affected / exposed	4 / 45 (8.89%)			
occurrences (all)	4			
Neutrophil count decreased				
subjects affected / exposed	12 / 45 (26.67%)			
occurrences (all)	33			
Platelet count decreased				
subjects affected / exposed	9 / 45 (20.00%)			
occurrences (all)	21			
Prothrombin time abnormal				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			

Roseolovirus test positive subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
SARS-CoV-2 test negative subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Transaminases increased subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 3		
Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4		
Weight increased subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
White blood cell count decreased subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 10		
Injury, poisoning and procedural complications			
Anaphylactic transfusion reaction subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Post procedural contusion subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Post procedural haemorrhage subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 0		
Subcutaneous haematoma subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Cardiac disorders			
Ventricular fibrillation subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Bradycardia			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Cardiac failure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Sinus tachycardia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Nervous system disorders			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Post herpetic neuralgia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Restless legs syndrome			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Coagulopathy subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1			
Anaemia subjects affected / exposed occurrences (all)	21 / 45 (46.67%) 36			
Febrile neutropenia subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2			
Hyperleukocytosis subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1			
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1			
Leukocytosis subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1			
Leukopenia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3			
Lymphopenia subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1			
Thrombocytopenia subjects affected / exposed occurrences (all)	9 / 45 (20.00%) 9			
Thrombotic microangiopathy subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1			
Neutropenia subjects affected / exposed occurrences (all)	9 / 45 (20.00%) 17			
Eye disorders Dry eye				

subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Eye disorder			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	5		
Angular cheilitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	6		
Intestinal haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	6		
Anal fissure			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Hypertransaminasaemia			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	3		
Hepatic steatosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Hirsutism			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Acne			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Bullous haemorrhagic dermatosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Dermatitis contact			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Ecchymosis			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Eczema asteatotic			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Night sweats			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		

Pain of skin			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Purpura			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin fissures			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Skin striae			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Glycosuria			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Ketonuria			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	2		
Micturition urgency			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Polyuria			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Renal impairment			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Urinary tract pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Cushingoid			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Amyotrophy			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Muscle contracture			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Osteopenia			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	4		
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Bacteraemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	3		
Cytomegalovirus infection			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	4		
Fungal infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	4		
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	3		

Ear infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Epstein-Barr virus infection				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences (all)	2			
Epstein-Barr virus infection reactivation				
subjects affected / exposed	4 / 45 (8.89%)			
occurrences (all)	4			
Fungal foot infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Cytomegalovirus infection reactivation				
subjects affected / exposed	4 / 45 (8.89%)			
occurrences (all)	5			
Herpes simplex				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Klebsiella infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Mucosal infection				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences (all)	2			
Nail infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Oral candidiasis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Urinary tract infection				

subjects affected / exposed	2 / 45 (4.44%)			
occurrences (all)	2			
Otitis externa				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Otitis media				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences (all)	2			
Sinusitis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Staphylococcal sepsis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Varicella zoster virus infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Viraemia				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Viral haemorrhagic cystitis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Vulvovaginal mycotic infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences (all)	1			
Vulvovaginitis				

subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Central obesity			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Decreased appetite			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Folate deficiency			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hyperferritinaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Hypoalbuminaemia			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	9		
Hypoglycaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	8 / 45 (17.78%)		
occurrences (all)	7		
Hypomagnesaemia			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		

Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Hypophosphataemia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 4		
Metabolic acidosis subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2019	The main purpose of this amendment was to broaden the eligible subject populations, modify study assessment and revise safety dose modifications based on feedback from investigators on current practices in the management of acute GvHD. The number of subjects was expanded to a total of 45 subjects treated at the RP2D, thus increasing the number of subjects for safety and efficacy evaluation.
14 October 2020	The main purpose of amendment 2 was to update the guidelines regarding the management of ruxolitinib based on liver monitoring laboratory results, to update the inclusion criteria to allow for nasogastric tube administration of the pediatric formulation, to provide clarifications regarding the management of ruxolitinib tapering, to update contraception guidelines and pregnancy reporting requirements for female subjects of child-bearing potential and to clarify requirements for ruxolitinib post-trial access. The assessment of benefit and risk related to SARS-CoV-2 virus and the COVID-19 pandemic determined no substantial additional risk for subject safety at this time.
22 June 2022	The main purpose of this amendment to include public health emergency disruption proofing language, to provide guidance on subject management, including withdrawal of consent, and to decrease the minimum enrollment requirements of treatment-naïve subjects from 40% to at least 20% due to recruitment challenges. The sample remains representative of the study population and therefore the sample size was not re-estimated due to this modification.

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: