



## Clinical trial results:

### A Phase 2a, Open-label, Single and Multiple Dose Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Treatment Effect of GBT440 in Pediatric Participants with Sickle Cell Disease

#### Summary

EudraCT number	2016-004209-15
Trial protocol	GB
Global end of trial date	02 October 2023

#### Results information

Result version number	v1 (current)
This version publication date	13 June 2025
First version publication date	13 June 2025

#### Trial information

##### Trial identification

Sponsor protocol code	C5341020
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02850406
WHO universal trial number (UTN)	-
Other trial identifiers	GBT440-007: Pfizer Protocol Number

Notes:

#### Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Boulevard East, New York, United States, NY 10001-2192
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002356-PIP02-20
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	12 December 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 October 2023
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

Part A: To characterize the pharmacokinetic (PK) of voxelotor in plasma and whole blood following a single dose in pediatric participants with sickle cell disease (SCD).

Part B: To assess the efficacy of voxelotor in pediatric participants with SCD as measured by improvement in anemia.

Part C: To evaluate the effect of voxelotor on cerebral hemodynamics in pediatric participants with SCD with elevated or conditional transcranial Doppler (TCD) flow velocity as assessed by TCD ultrasonography.

Part D: To evaluate the safety and tolerability of voxelotor in pediatric participants with SCD aged 6 months to < 4 years.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2016
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	Lebanon: 38
Country: Number of subjects enrolled	United States: 95
Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	147
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	89
Adolescents (12-17 years)	58
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

This study consisted of four parts-Part A, B, C and D. The study was terminated as the emerging clinical data indicated that the risk profile of voxelotor in people with sickle cell disease (SCD) exceeded the benefits observed in previously generated global research and required further assessment.

### Pre-assignment

Screening details:

A total of 147 pediatric participants with SCD (13 in Part A, 40 in Part B, 62 in Part C and 32 in Part D) were enrolled in the study.

### Period 1

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

Blinding implementation details:

NA

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg

Arm description:

Participants aged 12 to 17 years received a single oral dose of voxelotor 600 milligrams (mg) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose of voxelotor capsules or tablets were administered.

<b>Arm title</b>	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg
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Arm description:

Participants aged 6 to 11 years received a single oral dose of voxelotor 600 mg on Day 1.

Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Single oral dose of granulation from voxelotor capsules were mixed with food and administered.

<b>Arm title</b>	Part B: Voxelotor 900 mg QD
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Arm description:

Participants aged 12 to 17 years received once daily (QD) oral dose of voxelotor 900 mg for 24 weeks.

Arm type	Experimental
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Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use
Dosage and administration details:	
Single oral dose of voxelotor capsules or tablets were administered.	
<b>Arm title</b>	Part B: Voxelotor 1500 mg QD
Arm description:	
Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 24 weeks.	
Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use
Dosage and administration details:	
Single oral dose of voxelotor capsules or tablets were administered.	
<b>Arm title</b>	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD
Arm description:	
Participants aged 4 to 11 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet, Powder for oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Voxelotor 1500 mg/day equivalent based on body weight administered for 48 weeks.	
<b>Arm title</b>	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD
Arm description:	
Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet, Powder for oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Voxelotor 1500 mg/day administered for 48 weeks.	
<b>Arm title</b>	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD
Arm description:	
Participants aged 6 months (M) to <2 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Voxelotor 1500 mg/day equivalent based on body weight administered for 48 weeks.

<b>Arm title</b>	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD
Arm description: Participants aged 2 to <4 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Arm type	Experimental
Investigational medicinal product name	Voxelotor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Voxelotor 1500 mg/day equivalent based on body weight administered for 48 weeks.

<b>Number of subjects in period 1</b>	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg	Part B: Voxelotor 900 mg QD
Started	7	6	25
Completed	7	6	22
Not completed	0	0	3
Consent withdrawn by subject	-	-	1
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Non-compliance	-	-	1
Unspecified	-	-	-
Lost to follow-up	-	-	1

<b>Number of subjects in period 1</b>	Part B: Voxelotor 1500 mg QD	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD
Started	15	51	11
Completed	12	39	3
Not completed	3	12	8
Consent withdrawn by subject	2	6	3
Physician decision	-	1	-
Adverse event, non-fatal	1	4	2
Non-compliance	-	-	-
Unspecified	-	1	3
Lost to follow-up	-	-	-

<b>Number of subjects in period 1</b>	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD
Started	9	23
Completed	7	20
Not completed	2	3
Consent withdrawn by subject	-	1
Physician decision	1	1
Adverse event, non-fatal	1	-
Non-compliance	-	-
Unspecified	-	1
Lost to follow-up	-	-

## Baseline characteristics

### Reporting groups

Reporting group title	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg
Reporting group description:	
Participants aged 12 to 17 years received a single oral dose of voxelotor 600 milligrams (mg) on Day 1.	
Reporting group title	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg
Reporting group description:	
Participants aged 6 to 11 years received a single oral dose of voxelotor 600 mg on Day 1.	
Reporting group title	Part B: Voxelotor 900 mg QD
Reporting group description:	
Participants aged 12 to 17 years received once daily (QD) oral dose of voxelotor 900 mg for 24 weeks.	
Reporting group title	Part B: Voxelotor 1500 mg QD
Reporting group description:	
Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 24 weeks.	
Reporting group title	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD
Reporting group description:	
Participants aged 4 to 11 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Reporting group title	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD
Reporting group description:	
Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Reporting group title	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD
Reporting group description:	
Participants aged 6 months (M) to <2 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Reporting group title	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD
Reporting group description:	
Participants aged 2 to <4 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	

Reporting group values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg	Part B: Voxelotor 900 mg QD
Number of subjects	7	6	25
Age Categorical			
Units: Subjects			

Age continuous			
Units: Years			
arithmetic mean	15.4	8.2	14.0
standard deviation	± 0.79	± 1.72	± 1.68
Gender categorical			
Units: Subjects			
Male	4	3	11
Female	3	3	14
Race/Ethnicity, Customized			
Units: Subjects			
Arab/Middle Eastern	0	1	0
Black or African American	3	3	18



White	2	2	6
Multi-racial	2	0	1
Middle Eastern or North African	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	7	6	24

Reporting group values	Part B: Voxelotor 1500 mg QD	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD
Number of subjects	15	51	11
Age Categorical Units: Subjects			

Age continuous Units: Years			
arithmetic mean	13.9	7.3	13.1
standard deviation	± 1.58	± 2.06	± 1.04
Gender categorical Units: Subjects			
Male	10	27	4
Female	5	24	7
Race/Ethnicity, Customized Units: Subjects			
Arab/Middle Eastern	0	0	0
Black or African American	11	44	11
White	4	3	0
Multi-racial	0	0	0
Middle Eastern or North African	0	4	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	3	0
Not Hispanic or Latino	14	48	11

Reporting group values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD	Total
Number of subjects	9	23	147
Age Categorical Units: Subjects			

Age continuous Units: Years			
arithmetic mean	1.4	3.0	-
standard deviation	± 0.41	± 0.51	
Gender categorical Units: Subjects			
Male	3	9	71
Female	6	14	76

Race/Ethnicity, Customized			
Units: Subjects			
Arab/Middle Eastern	0	0	1
Black or African American	5	9	104
White	2	9	28
Multi-racial	2	0	5
Middle Eastern or North African	0	5	9
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	7
Not Hispanic or Latino	8	22	140

## End points

### End points reporting groups

Reporting group title	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg
Reporting group description: Participants aged 12 to 17 years received a single oral dose of voxelotor 600 milligrams (mg) on Day 1.	
Reporting group title	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg
Reporting group description: Participants aged 6 to 11 years received a single oral dose of voxelotor 600 mg on Day 1.	
Reporting group title	Part B: Voxelotor 900 mg QD
Reporting group description: Participants aged 12 to 17 years received once daily (QD) oral dose of voxelotor 900 mg for 24 weeks.	
Reporting group title	Part B: Voxelotor 1500 mg QD
Reporting group description: Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 24 weeks.	
Reporting group title	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD
Reporting group description: Participants aged 4 to 11 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Reporting group title	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD
Reporting group description: Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Reporting group title	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD
Reporting group description: Participants aged 6 months (M) to <2 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	
Reporting group title	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD
Reporting group description: Participants aged 2 to <4 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.	

### Primary: Part A: Maximum Concentration (Cmax) of Voxelotor in Whole Blood

End point title	Part A: Maximum Concentration (Cmax) of Voxelotor in Whole Blood <sup>[1][2]</sup>
End point description: Pharmacokinetic (PK) population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma.	
End point type	Primary
End point timeframe: pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose	

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

[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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)	24300 ( $\pm$ 36.39)	47300 ( $\pm$ 43.62)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Voxelotor in Whole Blood

End point title	Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Voxelotor in Whole Blood <sup>[3][4]</sup>
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End point description:

AUC0-last was calculated using the linear/log trapezoid rule. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma.

End point type	Primary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

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

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	1570000 ( $\pm$ 38.13)	2540000 ( $\pm$ 50.25)		

## Statistical analyses

No statistical analyses for this end point

**Primary: Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor in Whole Blood**

End point title	Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor in Whole Blood <sup>[5]</sup> <sup>[6]</sup>
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End point description:

AUC0-inf was calculated as AUCt + Ct/lambdaz, where AUCt=area under the concentration-time curve at designated time, Ct is the last quantifiable concentration for whole blood and lambdaz=elimination rate constant. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma.

End point type	Primary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96,168 and 336 hours post-dose

Notes:

[5] - 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: The end point is specific to Part A; hence, only Part A arms are reported.

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

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	1520000 (± 40.98)	2570000 (± 50.59)		

**Statistical analyses**

No statistical analyses for this end point

**Primary: Part B: Change From Baseline to Week 24 in Hemoglobin Level**

End point title	Part B: Change From Baseline to Week 24 in Hemoglobin
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Overall Number of Participants Analyzed' signifies number of participants evaluable for this outcome measure.

End point type	Primary
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End point timeframe:

Baseline, Week 24

Notes:

[7] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

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

Justification: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	12		
Units: Gram per deciliter				
arithmetic mean (standard deviation)	0.7 (± 0.86)	0.2 (± 1.02)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Part C: Change From Baseline to Week 48 in Cerebral Blood Flow

End point title	Part C: Change From Baseline to Week 48 in Cerebral Blood Flow <sup>[9][10]</sup>
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End point description:

Cerebral blood flow was measured using transcranial Doppler (TCD) sonography. Change from baseline in cerebral blood flow as measured by the time-averaged mean of the maximum (TAMM) TCD velocity is reported. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Overall Number of Participants Analyzed' signifies number of participants evaluable for this outcome measure.

End point type	Primary
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End point timeframe:

Baseline, Week 48

Notes:

[9] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

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

Justification: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	3		
Units: Centimeter per second				
arithmetic mean (standard deviation)	-0.4 (± 16.76)	-26.3 (± 11.59)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Part D: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Part D: Number of Participants With Treatment Emergent
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## End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant administered a pharmaceutical product during the course of a clinical investigation. TEAE was defined as an AE that emerged on or after initiation of study drug (having been absent pre-treatment), or an AE that existed pre-treatment and worsened on treatment (relative to the pre-treatment state) through 28 days after study drug discontinuation. An SAE was any AE that resulted in any of the following outcomes: death, life threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, congenital anomaly or birth defect, other important medical events. AEs were classified as SCD-related and non-SCD related. Safety population comprised of all participants who received any amount of study drug.

## End point type

Primary

## End point timeframe:

From start of study treatment up to 28 days after study treatment discontinuation (Up to 52 weeks)

## Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The end point is specific to Part D; hence, only Part D arms are reported.

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

Justification: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	23		
Units: Participants				
Non-SCD related TEAEs	9	20		
Non-SCD related SAEs	6	12		
SCD related TEAEs	6	14		
SCD related SAEs	3	9		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Maximum Concentration (Cmax) of Voxelotor in Plasma

## End point title

Part A: Maximum Concentration (Cmax) of Voxelotor in Plasma  
[13]

## End point description:

PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

## End point type

Secondary

## End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

## Notes:

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

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)	1880 ( $\pm$ 32.49)	3390 ( $\pm$ 37.82)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Maximum Concentration (Cmax) of Voxelotor in Red Blood Cells (RBC)

End point title	Part A: Maximum Concentration (Cmax) of Voxelotor in Red Blood Cells (RBC) <sup>[14]</sup>
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End point description:

PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)	91500 ( $\pm$ 33.17)	168000 ( $\pm$ 35.56)		

## Statistical analyses



**Secondary: Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Voxelotor in Plasma**

End point title	Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Voxelotor in Plasma <sup>[15]</sup>
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## End point description:

AUC0-last was calculated using the linear/log trapezoid rule. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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## End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

## 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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	104000 (± 20.85)	148000 (± 38.69)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Voxelotor in RBC**

End point title	Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Voxelotor in RBC <sup>[16]</sup>
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## End point description:

AUC0-last was calculated using the linear/log trapezoid rule. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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## End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

## 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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	6070000 ( $\pm$ 28.69)	8950000 ( $\pm$ 47.05)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor in Plasma

End point title	Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor in Plasma <sup>[17]</sup>
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End point description:

AUC0-inf was calculated as  $AUC_t + C_t/\lambda_{daz}$ , where  $AUC_t$ =area under the concentration-time curve at designated time,  $C_t$  is the last quantifiable concentration for plasma and  $\lambda_{daz}$  is the elimination rate constant. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	101000 ( $\pm$ 20.51)	150000 ( $\pm$ 38.01)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor in RBC

End point title	Part A: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor in RBC <sup>[18]</sup>
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End point description:

AUC0-inf was calculated as AUCt + Ct/lambdaz, where AUCt=area under the concentration-time curve at designated time, Ct is the last quantifiable concentration and lambdaz is the elimination rate constant. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	5550000 (± 24.31)	9070000 (± 47.47)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Time at Which Cmax Was Observed (Tmax) for Voxelotor in Whole Blood

End point title	Part A: Time at Which Cmax Was Observed (Tmax) for Voxelotor in Whole Blood <sup>[19]</sup>
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End point description:

PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

Notes:

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

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Hours				
median (full range (min-max))	24.2 (7.67 to 49.9)	8.73 (7.78 to 25.3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Time at Which Cmax Was Observed (Tmax) for Voxelotor in RBC

End point title	Part A: Time at Which Cmax Was Observed (Tmax) for Voxelotor in RBC <sup>[20]</sup>
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End point description:

PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Hours				
median (full range (min-max))	9.00 (7.67 to 49.9)	8.75 (8.72 to 25.3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Time at Which Cmax Was Observed (Tmax) for Voxelotor in Plasma

End point title	Part A: Time at Which Cmax Was Observed (Tmax) for Voxelotor in Plasma <sup>[21]</sup>
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End point description:

PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type Secondary

End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

Notes:

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

Justification: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: Hours				
median (full range (min-max))	2.83 (1.95 to 9.00)	2.83 (2.57 to 8.72)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Terminal Elimination Half-Life (T1/2) for Voxelotor in Whole Blood

End point title Part A: Terminal Elimination Half-Life (T1/2) for Voxelotor in Whole Blood<sup>[22]</sup>

End point description:

T1/2 was the time measured for the drug concentration to decrease by one half. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type Secondary

End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		

Units: Hours				
geometric mean (geometric coefficient of variation)	31.9 (± 18.76)	28.5 (± 26.18)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Terminal Elimination Half-Life (T1/2) for Voxelotor in Plasma

End point title	Part A: Terminal Elimination Half-Life (T1/2) for Voxelotor in Plasma <sup>[23]</sup>
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End point description:

T1/2 was the time measured for the drug concentration to decrease by one half. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

Notes:

[23] - 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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Hours				
geometric mean (geometric coefficient of variation)	46.4 (± 6.40)	40.7 (± 31.48)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Terminal Elimination Half-Life (T1/2) for Voxelotor in RBC

End point title	Part A: Terminal Elimination Half-Life (T1/2) for Voxelotor in RBC <sup>[24]</sup>
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End point description:

T1/2 was the time measured for the drug concentration to decrease by one half. PK population comprised of all participants who received any amount of study drug and who provided PK data from at least one post-dose sample in plasma. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

pre-dose, 2, 8, 24, 48, 96, 168 and 336 hours post-dose

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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: Hours				
geometric mean (geometric coefficient of variation)	28.8 (± 12.89)	27.3 (± 30.95)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Percentage Hemoglobin (Hb) Occupancy

End point title	Part A: Percentage Hemoglobin (Hb) Occupancy <sup>[25]</sup>
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End point description:

Percentage hemoglobin occupancy (% Hb Occupancy) refers to the percentage of hemoglobin molecules within red blood cells that were bound to study drug. Concentration of voxelotor in whole blood and plasma was used to calculate %Hb occupancy. Percentage Hb occupancy within RBCs was estimated using the formula:

$$([\text{Concentration of voxelotor in whole blood} - \{1 - \text{hematocrit}\}] * [\text{Concentration of voxelotor in plasma} / \text{hematocrit}]) / 5000 * 100$$
  
Data was not collected as the model for Hb occupancy within RBCs was not developed for single dose administration (Part A).

End point type	Secondary
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End point timeframe:

Day 28

Notes:

[25] - 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: The end point is specific to Part A; hence, only Part A arms are reported.

End point values	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 <sup>[26]</sup>	0 <sup>[27]</sup>		
Units: Percentage of bound hemoglobin				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[26] - Model for Hb occupancy within RBC not developed for single dose administration (Part A).

[27] - Model for Hb occupancy within RBC not developed for single dose administration (Part A).

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percentage of Days With SCD Symptom Exacerbation During the First 24 Weeks of Treatment

End point title	Part B: Percentage of Days With SCD Symptom Exacerbation During the First 24 Weeks of Treatment <sup>[28]</sup>
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End point description:

SCD symptoms were measured using the Sickle Cell Disease Severity Measure (SCDSM) which was a self-administered 9-item questionnaire of SCD core symptoms including pain severity, frequency, and type, as well as fatigue and mental acuity, on a 4-point response scale that was completed daily using a handheld electronic device by the participants. Data for this outcome measure was not collected as the definition for this variable was not available at the time of analysis.

End point type	Secondary
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End point timeframe:

From Day 1 up to 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 <sup>[29]</sup>	0 <sup>[30]</sup>		
Units: Percentage of days				
number (not applicable)				

Notes:

[29] - Data not collected as variable was not defined at time of analysis.

[30] - Data not collected as variable was not defined at time of analysis.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Change from Baseline to Week 21 to 24 in the Sickle Cell Disease Severity Measure (SCDSM) Total Symptom Score (TSS)

End point title	Part B: Change from Baseline to Week 21 to 24 in the Sickle Cell Disease Severity Measure (SCDSM) Total Symptom Score (TSS) <sup>[31]</sup>
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End point description:

The SCDSM was a self-administered 9-item questionnaire of SCD core symptoms including pain severity, frequency, and type, as well as fatigue and mental acuity, on a 4-point response scale with a range of 0 (strongly disagree) to 4 (strongly agree) that was completed daily using a handheld electronic device by the participants. TSS was calculated as the sum of the 9-item questionnaire scores scaled to a 100-point scale with a range of 0 (no symptoms) to 100 (most severe symptoms). Baseline TSS was the average



of the non-missing score during the Screening period. The average of change from baseline in SCDsM TSS score for the 4-week period (Week 21 to 24) is reported. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 21 to 24	

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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8		
Units: Units on a scale				
arithmetic mean (standard deviation)	6.4 (± 17.98)	-10.7 (± 18.70)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Percent Change From Baseline to Weeks 12 and 24 in Lactate Dehydrogenase (LDH)

End point title	Part B: Percent Change From Baseline to Weeks 12 and 24 in Lactate Dehydrogenase (LDH)
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 12 and 24	

Notes:

[32] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	14		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 12	-6.3 (± 21.08)	-1.7 (± 32.78)		
Week 24	-6.3 (± 22.47)	-1.9 (± 14.59)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percent Change From Baseline to Weeks 12 and 24 in Indirect Bilirubin

End point title	Part B: Percent Change From Baseline to Weeks 12 and 24 in Indirect Bilirubin <sup>[33]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12 and 24

Notes:

[33] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	13		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 12; n=22, 13	-32.1 (± 31.98)	-29.9 (± 33.59)		
Week 24; n=22, 12	-37.5 (± 29.07)	-32.1 (± 31.53)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Percent Change From Baseline to Week 12 and 24 in Percentage Reticulocytes

End point title	Part B: Percent Change From Baseline to Week 12 and 24 in Percentage Reticulocytes <sup>[34]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this outcome measure and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12 and 24

Notes:

[34] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	14		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 12; n=23, 14	-8.7 (± 36.46)	-3.5 (± 42.96)		
Week 24; n=22, 12	-14.1 (± 34.06)	1.5 (± 43.18)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Cmax of Voxelotor in Whole Blood and Plasma

End point title | Part B: Cmax of Voxelotor in Whole Blood and Plasma<sup>[35]</sup>

End point description:

PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information.

End point type | Secondary

End point timeframe:

Day 1 (pre-dose, 2, 8, 24 hours post-dose), pre-dose on Weeks 2, 4, 8, 12, 16, 20 and 24

Notes:

[35] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	15		
Units: Microgram per milliliter				
geometric mean (geometric coefficient of variation)				
Cmax, plasma	5.64 (± 41)	9.81 (± 37)		
Cmax, whole blood	102 (± 38)	59 (± 32)		

## Statistical analyses

**Secondary: Part B: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC<sub>0-inf</sub>) of Voxelotor for Whole Blood and Plasma**

End point title	Part B: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC <sub>0-inf</sub> ) of Voxelotor for Whole Blood and Plasma <sup>[36]</sup>
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## End point description:

AUC<sub>0-inf</sub> was calculated as AUC<sub>t</sub> + C<sub>t</sub>/λ<sub>bd</sub>, where AUC<sub>t</sub>=area under the concentration-time curve at designated time, C<sub>t</sub> is the last quantifiable concentration and λ<sub>bd</sub> is the elimination rate constant. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information.

End point type	Secondary
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## End point timeframe:

Day 1 (pre-dose, 2, 8, 24 hours post-dose), pre-dose on Weeks 2, 4, 8, 12, 16, 20 and 24

## Notes:

[36] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	15		
Units: Hours*microgram per milliliter				
geometric mean (geometric coefficient of variation)				
AUC <sub>0-inf</sub> , plasma	113 (± 46)	195 (± 40)		
AUC <sub>0-inf</sub> , whole blood	2090 (± 43)	3290 (± 36)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part B: Terminal Elimination Half-life of Voxelotor for Plasma and Whole Blood**

End point title	Part B: Terminal Elimination Half-life of Voxelotor for Plasma and Whole Blood <sup>[37]</sup>
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## End point description:

T<sub>1/2</sub> was the time measured for the drug concentration to decrease by one half. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information.

End point type	Secondary
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## End point timeframe:

Day 1 (pre-dose, 2, 8, 24 hours post-dose), pre-dose on Weeks 2, 4, 8, 12, 16, 20 and 24

## Notes:

[37] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	15		
Units: Hours				
geometric mean (geometric coefficient of variation)				
T1/2, plasma	33 (± 41)	33.9 (± 44)		
T1/2, whole blood	31.1 (± 39)	31.4 (± 41)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Accumulation Ratio (Rac) of Voxelotor for Plasma and Whole Blood

End point title	Part B: Accumulation Ratio (Rac) of Voxelotor for Plasma and Whole Blood <sup>[38]</sup>
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End point description:

Accumulation ratio was calculated as ratio of area under the concentration-time curve from time zero (predose) to 24 hours (AUC0-24) at steady-state (Day 28) to AUC0-24 on Day 1. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information.

End point type	Secondary
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End point timeframe:

Day 1 (0 to 24 hours post-dose) and Day 28 (0 to 24 hours post-dose)

Notes:

[38] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	15		
Units: Ratio				
geometric mean (geometric coefficient of variation)				
Rac, plasma	2.57 (± 29)	2.62 (± 33)		
Rac, whole blood	2.46 (± 27)	2.47 (± 30)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Percentage Hemoglobin Occupancy

End point title	Part B: Percentage Hemoglobin Occupancy <sup>[39]</sup>
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**End point description:**

% Hb Occupancy refers to the percentage of hemoglobin molecules within red blood cells that were bound to study drug. Concentration of voxelotor in whole blood and plasma was used to calculate %Hb occupancy. Percentage Hb occupancy within RBCs was estimated using the formula:  $[(\text{Concentration of voxelotor in whole blood} - \{1 - \text{hematocrit}\}) * (\text{Concentration of voxelotor in plasma} / \text{hematocrit})] / 5000 * 100$ . PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information.

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End point type	Secondary
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End point timeframe:

Day 28

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**Notes:**

[39] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	15		
Units: Percentage of bound hemoglobin				
geometric mean (geometric coefficient of variation)	19.4 (± 34)	29.5 (± 27)		

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Part B: Change From Baseline to Week 12 and 24 in Cerebral Blood Flow as Measured by the TAMM TCD Velocity**

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End point title	Part B: Change From Baseline to Week 12 and 24 in Cerebral Blood Flow as Measured by the TAMM TCD Velocity <sup>[40]</sup>
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End point description:

Cerebral blood flow velocity was measured using TCD sonography. Change from baseline in cerebral blood flow velocity as measured by TAMM TCD velocity is reported. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

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End point type	Secondary
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End point timeframe:

Baseline, Weeks 12 and 24

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**Notes:**

[40] - 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: The end point is specific to Part B; hence, only Part B arms are reported.

End point values	Part B: Voxelotor 900 mg QD	Part B: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	13		
Units: Centimeter per second				
geometric mean (geometric coefficient of variation)				
Week 12; n=23, 13	0.9 (± 16.48)	-0.1 (± 9.34)		
Week 24; n=20, 12	-2.1 (± 14.03)	1.7 (± 14.26)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part C: Change From Baseline to Weeks 24 and 48 in Hemoglobin Level

End point title	Part C: Change From Baseline to Weeks 24 and 48 in Hemoglobin Level <sup>[41]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24 and 48

Notes:

[41] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	6		
Units: Grams per deciliter				
arithmetic mean (standard deviation)				
Week 24; n=41, 6	1.0 (± 1.16)	0.8 (± 1.14)		
Week 48; n=37, 3	0.7 (± 1.15)	-0.1 (± 0.20)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part C: Percent Change From Baseline to Weeks 24 and 48 in LDH

End point title	Part C: Percent Change From Baseline to Weeks 24 and 48 in LDH <sup>[42]</sup>
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**End point description:**

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
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**End point timeframe:**

Baseline, Weeks 24 and 48

**Notes:**

[42] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

<b>End point values</b>	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	4		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 24; n=39, 4	-5.1 (± 21.95)	-22.4 (± 22.08)		
Week 48; n=35, 2	-1.8 (± 23.80)	3.9 (± 8.91)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part C: Percent Change From Baseline to Weeks 24 and 48 in Indirect Bilirubin**

End point title	Part C: Percent Change From Baseline to Weeks 24 and 48 in Indirect Bilirubin <sup>[43]</sup>
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**End point description:**

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
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**End point timeframe:**

Baseline, Weeks 24 and 48

**Notes:**

[43] - 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: The end point is specific to Part C; hence, only Part C arms are reported.



End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	6		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 24; n=34, 6	-36.9 (± 26.55)	-45.7 (± 24.93)		
Week 48; n=32, 3	-26.6 (± 37.05)	-33.0 (± 36.76)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part C: Percent Change From Baseline to Weeks 24 and 48 in Percentage Reticulocytes

End point title	Part C: Percent Change From Baseline to Weeks 24 and 48 in Percentage Reticulocytes <sup>[44]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies number of participants evaluable for the specified rows.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24 and 48

Notes:

[44] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	5		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 24; n=37, 5	-4.76 (± 42.999)	-1.17 (± 31.595)		
Week 48; n=34, 2	-0.33 (± 46.353)	2.94 (± 38.295)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part C: Change From Baseline to Week 24 in Cerebral Blood Flow as Measured by the TAMM TCD Velocity

End point title	Part C: Change From Baseline to Week 24 in Cerebral Blood Flow as Measured by the TAMM TCD Velocity <sup>[45]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[45] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	6		
Units: Centimeter per second				
arithmetic mean (standard deviation)	-3.2 (± 15.69)	-11.8 (± 18.82)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part C: Time to Initial Hemoglobin Response

End point title	Part C: Time to Initial Hemoglobin Response <sup>[46]</sup>
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End point description:

Time to initial Hb response was defined as the time from first dose of study treatment to the first occurrence of a change from baseline in Hb > 1 gram per deciliter (g/dL). Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

From first dose of study treatment (Day 1) up to Week 48

Notes:

[46] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	8		
Units: Weeks				
arithmetic mean (standard deviation)	4.9 (± 5.51)	5.6 (± 4.90)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part C: Cmax of Voxelotor for Plasma and Whole Blood

End point title	Part C: Cmax of Voxelotor for Plasma and Whole Blood <sup>[47]</sup>
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End point description:

PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Day 1 (15 minutes to 2 hours post-dose), pre-dose on Weeks 4, 8, 12, 16, 20, 24, 36 and 48

Notes:

[47] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	11		
Units: Microgram per milliliter				
geometric mean (geometric coefficient of variation)				
Cmax, plasma	7.83 (± 61)	9.04 (± 43)		
Cmax, whole blood	127 (± 52)	137 (± 38)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part C: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor for Whole Blood and Plasma

End point title	Part C: Area Under the Concentration-Time Curve (AUC) From
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## End point description:

AUC0-inf was calculated as AUCt + Ct/lambdaz, where AUCt=area under the concentration-time curve at designated time, Ct is the last quantifiable concentration and lambdaz is the elimination rate constant. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies participants evaluable for this endpoint.

## End point type

Secondary

## End point timeframe:

Day 1 (15 minutes to 2 hours post-dose), pre-dose on Weeks 4, 8, 12, 16, 20, 24, 36 and 48

## Notes:

[48] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	11		
Units: Hours*microgram per milliliter				
geometric mean (geometric coefficient of variation)				
AUC0-inf, plasma	160 (± 72)	184 (± 44)		
AUC0-inf, whole blood	2660 (± 64)	2880 (± 41)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part C: Terminal Elimination Half-life (T1/2) of Voxelotor for Whole Blood and Plasma

## End point title

Part C: Terminal Elimination Half-life (T1/2) of Voxelotor for Whole Blood and Plasma<sup>[49]</sup>

## End point description:

T1/2 was the time measured for the drug concentration to decrease by one half in whole blood and plasma, respectively. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies participants evaluable for this endpoint.

## End point type

Secondary

## End point timeframe:

Day 1 (15 minutes to 2 hours post-dose), pre-dose on Weeks 4, 8, 12, 16, 20, 24, 36 and 48

## Notes:

[49] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	11		
Units: Hours				
geometric mean (geometric coefficient of variation)				
T1/2, plasma	41.6 (± 50)	35.6 (± 28)		
T1/2, whole blood	37.4 (± 48)	32.7 (± 25)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part C: Percentage Hemoglobin Occupancy of Voxelotor

End point title	Part C: Percentage Hemoglobin Occupancy of Voxelotor <sup>[50]</sup>
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End point description:

% Hb Occupancy refers to the percentage of hemoglobin molecules within red blood cells that were bound to study drug. Concentration of voxelotor in whole blood and plasma was used to calculate %Hb occupancy. Percentage Hb occupancy within RBCs was estimated using the formula:  

$$([\text{Concentration of voxelotor in whole blood} - \{1 - \text{hematocrit}\}] * [\text{Concentration of voxelotor in plasma} / \text{hematocrit}]) / 5000 * 100$$
 PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Day 28

Notes:

[50] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	11		
Units: Percentage of bound hemoglobin				
geometric mean (geometric coefficient of variation)	24.7 (± 47)	27.7 (± 30)		

## Statistical analyses

**Secondary: Part C: Percentage of Participants With Normal Transcranial Doppler (TCD) Flow Velocity at Week 48**

End point title	Part C: Percentage of Participants With Normal Transcranial Doppler (TCD) Flow Velocity at Week 48 <sup>[51]</sup>
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## End point description:

Normal TCD flow velocity was considered as < 170 centimeter per second (cm/sec) by non-imaging TCD or < 155 cm/sec by imaging transcranial Doppler (TCDi). Percentage of participants with normal TCD flow velocity at Week 48 by Baseline TCD group (i.e. Baseline normal TCD [<170 cm/sec] and Baseline conditional TCD [ $\geq$ 170 cm/sec] is reported. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. All participants reported, 'Participants Analyzed' contributed data to the table; however, may not have evaluable data for each row. Here, 'n' signifies number of participants evaluable for each row.

End point type	Secondary
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## End point timeframe:

Week 48

## Notes:

[51] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	3		
Units: Percentage of participants				
number (not applicable)				
Baseline normal; n=27, 1	96.3	100		
Baseline conditional; n=7, 2	42.9	100		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Part C: Annualized Incidence Rate of Vaso-occlusive Crisis (VOC) Events**

End point title	Part C: Annualized Incidence Rate of Vaso-occlusive Crisis (VOC) Events <sup>[52]</sup>
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## End point description:

VOC events included preferred terms of sickle cell anaemia with crisis, acute chest syndrome, pneumonia necrotising and pneumonia. Annualized incidence rate was calculated as total number of events divided by total person years. Total person years=sum of participants treatment period in years, which covered the time from first dose to last dose. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug.

End point type	Secondary
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## End point timeframe:

Up to Week 48

Notes:

[52] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	11		
Units: VOC events per person year				
number (confidence interval 95%)	1.246 (0.912 to 1.662)	2.250 (1.123 to 4.025)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Cmax of Voxelotor for Plasma and Whole Blood

End point title	Part D: Cmax of Voxelotor for Plasma and Whole Blood <sup>[53]</sup>
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End point description:

PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Day 1 (anytime between 15 minutes to 2 hours post-dose), pre-dose on Weeks 2, 8, 12, 16, 24, 36 and 48

Notes:

[53] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	21		
Units: Microgram per milliliter				
geometric mean (geometric coefficient of variation)				
Cmax, plasma	5.01 (± 73)	9.45 (± 34)		
Cmax, whole blood	87.2 (± 74)	149 (± 30)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part C: Annualized Incidence Rate of Stroke Events

End point title	Part C: Annualized Incidence Rate of Stroke Events <sup>[54]</sup>
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End point description:

Annualized incidence rate was calculated as total number of events divided by total person years. Total person years=sum of participants treatment period in years, which covered the time from first dose to last dose. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to Week 48

Notes:

[54] - 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: The end point is specific to Part C; hence, only Part C arms are reported.

End point values	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	11		
Units: Stroke events per person year				
number (confidence interval 95%)	0.000 (0.000 to 0.100)	0.000 (0.000 to 0.754)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part D: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor for Plasma and Whole Blood

End point title	Part D: Area Under the Concentration-Time Curve (AUC) From Time 0 Extrapolated to Infinity (AUC0-inf) of Voxelotor for Plasma and Whole Blood <sup>[55]</sup>
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End point description:

AUC0-inf was calculated as  $AUC_t + C_t/\lambda_{dz}$ , where  $AUC_t$ =area under the concentration-time curve at designated time,  $C_t$  is the last quantifiable concentration and  $\lambda_{dz}$  is the elimination rate constant. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies number of participants



evaluable for this endpoint

End point type	Secondary
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End point timeframe:

Day 1 (anytime between 15 minutes to 2 hours post-dose), pre-dose on Weeks 2, 8, 12, 16, 24, 36 and 48

Notes:

[55] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	21		
Units: Hours*microgram per milliliter				
geometric mean (geometric coefficient of variation)				
AUC0-inf, plasma	89.9 (± 110)	186 (± 38)		
AUC0-inf, whole blood	1600 (± 120)	3040 (± 36)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Percentage Hemoglobin Occupancy

End point title	Part D: Percentage Hemoglobin Occupancy <sup>[56]</sup>
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End point description:

% Hb Occupancy refers to the percentage of hemoglobin molecules within red blood cells that were bound to study drug. Concentration of voxelotor in whole blood and plasma was used to calculate %Hb occupancy. Percentage Hb occupancy within RBCs was estimated using the formula:

$$([\text{Concentration of voxelotor in whole blood} - \{1 - \text{hematocrit}\}] * [\text{Concentration of voxelotor in plasma} / \text{hematocrit}]) / 5000 * 100$$
PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Day 28

Notes:

[56] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	21		
Units: Percentage of bound hemoglobin				
geometric mean (geometric coefficient of variation)	17.5 (± 60)	28.9 (± 26)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: T1/2 of Voxelotor for Plasma and Whole Blood

End point title	Part D: T1/2 of Voxelotor for Plasma and Whole Blood <sup>[57]</sup>
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End point description:

T1/2 was the time measured for the drug concentration to decrease by one half. PK population comprised of participants who received at least one dose of voxelotor and had at least 1 measurable voxelotor concentration observation in plasma or whole blood with associated sampling time and dosing information. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Day 1 (anytime between 15 minutes to 2 hours post-dose), pre-dose on Weeks 2, 8, 12, 16, 24, 36 and 48

Notes:

[57] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	21		
Units: Hours				
geometric mean (geometric coefficient of variation)				
T1/2, plasma	24.1 (± 70)	36.1 (± 40)		
T1/2, whole blood	21.7 (± 82)	32.7 (± 38)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Change From Baseline to Weeks 24 and 48 in Hemoglobin Level

End point title	Part D: Change From Baseline to Weeks 24 and 48 in Hemoglobin Level <sup>[58]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24 and 48

Notes:

[58] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	20		
Units: Grams per deciliter				
arithmetic mean (standard deviation)				
Week 24	0.4 (± 2.03)	0.6 (± 1.02)		
Week 48	0.5 (± 1.53)	0.7 (± 1.45)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Percent Change From Baseline to Weeks 24 and 48 in LDH

End point title	Part D: Percent Change From Baseline to Weeks 24 and 48 in LDH <sup>[59]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies participants evaluable for the specified rows.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24 and 48

Notes:

[59] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	20		

Units: Percent change				
arithmetic mean (standard deviation)				
Week 24; n=6, 20	27.6 ( $\pm$ 56.46)	-0.4 ( $\pm$ 31.53)		
Week 48; n=6, 18	26.3 ( $\pm$ 43.98)	7.4 ( $\pm$ 45.94)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Percent Change From Baseline to Weeks 24 and 48 in Indirect Bilirubin

End point title	Part D: Percent Change From Baseline to Weeks 24 and 48 in Indirect Bilirubin <sup>[60]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies participants evaluable for the specified rows.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 24 and 48

Notes:

[60] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	18		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 24; n=7, 18	-14.4 ( $\pm$ 28.11)	-24.5 ( $\pm$ 24.50)		
Week 48; n=7, 17	4.4 ( $\pm$ 42.05)	-24.5 ( $\pm$ 21.97)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Percent Change From Baseline to Weeks 24 and 48 in Reticulocytes Count

End point title	Part D: Percent Change From Baseline to Weeks 24 and 48 in Reticulocytes Count <sup>[61]</sup>
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End point description:

Efficacy-Evaluable Population comprised of all participants who received any amount of study drug.

Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint and 'n' signifies participants evaluable for the specified rows

End point type	Secondary
End point timeframe:	
Baseline, Weeks 24 and 48	

Notes:

[61] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	14		
Units: Percent change				
arithmetic mean (standard deviation)				
Week 24; n=6, 14	-3.6 (± 28.64)	3.8 (± 31.88)		
Week 48; n=6, 13	-11.5 (± 31.19)	-0.7 (± 29.70)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part D: Time to Initial Hemoglobin Response

End point title	Part D: Time to Initial Hemoglobin Response <sup>[62]</sup>
End point description:	
Time to initial Hb response, defined as the time from first dose of study treatment to the first occurrence of a change from baseline in Hb > 1 g/dL. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug. Here, 'Participants Analyzed' signifies number of participants evaluable for this endpoint.	
End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to Week 48

Notes:

[62] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	18		
Units: Weeks				
arithmetic mean (standard deviation)	8.0 (± 7.60)	4.7 (± 8.80)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part D: Annualized Incidence Rate of VOC Events

End point title	Part D: Annualized Incidence Rate of VOC Events <sup>[63]</sup>
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End point description:

VOC events included preferred terms of 'Sickle cell anemia with crisis', 'Acute chest syndrome', 'Pneumonia necrotising,' and 'Pneumonia. Annualized incidence rate was calculated as total number of events divided by total person years. Total person years=sum of participants treatment period in years, which covered the time from first dose to last dose. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to Week 48

Notes:

[63] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

End point values	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	23		
Units: VOC events per person year				
number (confidence interval 95%)	1.473 (0.706 to 2.708)	1.399 (0.914 to 2.050)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part D: Annualized Incidence Rate of Stroke Events

End point title	Part D: Annualized Incidence Rate of Stroke Events <sup>[64]</sup>
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End point description:

Annualized incidence rate was calculated as total number of events divided by total person years. Total person years=sum of participants treatment period in years, which covered the time from first dose to last dose. Efficacy-Evaluable Population comprised of all participants who received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to Week 48

Notes:

[64] - 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: The end point is specific to Part D; hence, only Part D arms are reported.

<b>End point values</b>	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	23		
Units: Stroke events per person year				
number (confidence interval 95%)	0.000 (0.000 to 2.708)	0.000 (0.000 to 0.198)		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Part A: From start of treatment on Day 1 up to 2 weeks after last dose (up to Day 15); Part B, C and D: From start of treatment on Day 1 up to 4 weeks after last dose (up to Week 28 for Part B and up to Week 52 for Parts C and D).

Adverse event reporting additional description:

An AE term may be reported as both serious and non-serious AE but are distinct events. An AE may be serious for 1 participant and non-serious for another participant, or a participant may have experienced both a serious and non-serious episode of the same event. Safety population comprised of all participants who received any amount of study drug.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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### Reporting groups

Reporting group title	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg
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Reporting group description:

Participants aged 12 to 17 years received a single oral dose of voxelotor 600 milligrams (mg) on Day 1.

Reporting group title	Part B: Voxelotor 900 mg QD
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Reporting group description:

Participants aged 12 to 17 years received once daily (QD) oral dose of voxelotor 900 mg for 24 weeks.

Reporting group title	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg
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Reporting group description:

Participants aged 6 to 11 years received a single oral dose of voxelotor 600 mg on Day 1.

Reporting group title	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD
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Reporting group description:

Participants aged 6 months (M) to <2 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.

Reporting group title	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD
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Reporting group description:

Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.

Reporting group title	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD
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Reporting group description:

Participants aged 4 to 11 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.

Reporting group title	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg
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Reporting group description:

Participants aged 2 to <4 years received once daily oral dose of voxelotor 1500 mg for 48 weeks.

Reporting group title	Part B: Voxelotor 1500 mg QD
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Reporting group description:

Participants aged 12 to 17 years received once daily oral dose of voxelotor 1500 mg for 24 weeks.

<b>Serious adverse events</b>	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part B: Voxelotor 900 mg QD	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg
Total subjects affected by serious adverse events			



subjects affected / exposed	1 / 7 (14.29%)	12 / 25 (48.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Pallor	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Surgical and medical procedures			
Splenectomy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
General disorders and administration site conditions			
Pyrexia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Immune system disorders			
Hypersensitivity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Reproductive system and breast disorders			
Priapism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Respiratory, thoracic and mediastinal disorders			
Hypoxia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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

Acute chest syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (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
Pleural effusion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Investigations			
Haemoglobin decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Electrocardiogram T wave inversion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Ultrasound head abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 7 (14.29%)	9 / 25 (36.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 16	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemolytic anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Hypersplenism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Platelet disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Eye disorders			
Periorbital swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Gastrointestinal disorders			
Constipation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Vomiting	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Hepatobiliary disorders			
Cholecystitis acute	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Skin and subcutaneous tissue disorders			
Rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Pain in extremity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Infections and infestations			
Influenza	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (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
Tonsillitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Viral infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Pneumonia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (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
Salmonellosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Bacteraemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Bronchiolitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Bronchitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Malaria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Rotavirus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Sepsis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Pneumonia necrotising			
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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
Metabolism and nutrition disorders			
Dehydration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (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

<b>Serious adverse events</b>	Part D: Participants aged 6M to <2 years: Voxelotor 1500 mg QD	Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg QD	Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)	8 / 11 (72.73%)	23 / 51 (45.10%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Pallor	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Splenectomy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
General disorders and administration site conditions			
Pyrexia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 9 (22.22%)	1 / 11 (9.09%)	5 / 51 (9.80%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Priapism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Acute chest syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	8 / 51 (15.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram T wave inversion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (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
Ultrasound head abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	7 / 11 (63.64%)	18 / 51 (35.29%)
occurrences causally related to treatment / all	0 / 1	0 / 10	1 / 42
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemolytic anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Hypersplenism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	4 / 51 (7.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (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
Anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 9 (22.22%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Periorbital swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Vomiting	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Hepatobiliary disorders			
Cholecystitis acute	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		



subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Infections and infestations			
Influenza	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (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
Viral infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	3 / 51 (5.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (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
Bronchiolitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (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
Bronchitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (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
Malaria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (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
Rotavirus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (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	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (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
Pneumonia necrotising			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
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			

Dehydration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
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	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg	Part B: Voxelotor 1500 mg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 23 (60.87%)	7 / 15 (46.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Pallor	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Splenectomy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Priapism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 23 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute chest syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Haemoglobin decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave inversion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ultrasound head abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	7 / 23 (30.43%)	4 / 15 (26.67%)	
occurrences causally related to treatment / all	0 / 13	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemolytic anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersplenism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	4 / 23 (17.39%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Periorbital swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	3 / 23 (13.04%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia necrotising subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders Dehydration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part A: Participants aged 12 to 17 years: Voxelotor 600 mg	Part B: Voxelotor 900 mg QD	Part A: Participants aged 6 to 11 years: Voxelotor 600 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 7 (85.71%)	22 / 25 (88.00%)	3 / 6 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign lymph node neoplasm	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions Non-cardiac chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 7 (14.29%)	2 / 25 (8.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Pyrexia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	2 / 25 (8.00%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	2 / 25 (8.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Fatigue	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0



Chest discomfort	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Peripheral swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Gait disturbance	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Immune system disorders			
Seasonal allergy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Allergic oedema	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Reproductive system and breast disorders			
Priapism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	1	0
occurrences (all)			
Respiratory, thoracic and mediastinal disorders			
Acute chest syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	2 / 25 (8.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	2	0
occurrences (all)			
Cough	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	2	0
occurrences (all)			
Oropharyngeal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	1	0
occurrences (all)			

Nasal congestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Epistaxis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	2 / 25 (8.00%) 3	0 / 6 (0.00%) 0
Dyspnoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Rhinorrhoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Upper-airway cough syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Hypoxia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Sinus congestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Paranasal sinus hypersecretion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Obstructive sleep apnoea syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Tonsillar erythema	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Tonsillar hypertrophy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0

Allergic respiratory symptom subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1
Psychiatric disorders			
Stress	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Anxiety	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Insomnia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Mental status changes	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Post-traumatic stress disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Enuresis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Encopresis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Investigations			
Transaminases increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Bacterial test positive	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 25 (4.00%) 2	0 / 6 (0.00%) 0
Alanine aminotransferase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza A virus test positive	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ultrasound head abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Arthropod bite	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Joint injury	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laceration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Foot fracture	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epiphyseal fracture	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sports injury	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle strain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Foreign body ingestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ventricular hypertrophy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Left atrial dilatation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Diastolic dysfunction	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Cardiomegaly	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Nervous system disorders			
Headache	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 7 (14.29%)	7 / 25 (28.00%)
	occurrences (all)	1	10
Lethargy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Migraine	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)
	occurrences (all)	0	2
Syncope	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Dizziness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	3 / 25 (12.00%)
	occurrences (all)	0	3
Depressed level of consciousness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Hypersomnia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)
	occurrences (all)	0	0
Blood and lymphatic system disorders			

Sickle cell anaemia with crisis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 7 (14.29%) 1	5 / 25 (20.00%) 13	1 / 6 (16.67%) 1
Anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Neutropenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Thrombocytopenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	1 / 6 (16.67%) 1
Thrombocytosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Reticulocytopenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Splenomegaly	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Hypersplenism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Hypercoagulation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders			
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
Hypoacusis			
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Tinnitus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
Retinopathy sickle cell	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Visual impairment	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
Vomiting	0 / 7 (0.00%)	5 / 25 (20.00%)	0 / 6 (0.00%)
subjects affected / exposed	0	10	0
occurrences (all)			
Abdominal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	4 / 25 (16.00%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Nausea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 7 (28.57%)	9 / 25 (36.00%)	0 / 6 (0.00%)
occurrences (all)	2	12	0
Diarrhoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	3 / 25 (12.00%)	0 / 6 (0.00%)
occurrences (all)	0	5	0
Constipation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	3 / 25 (12.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Abdominal pain upper	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dental caries	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		



subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastritis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Abdominal distension	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
gastrointestinal disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip blister	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 7 (14.29%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholelithiasis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ocular icterus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertransaminasaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Jaundice	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Rash papular	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash generalised	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 7 (14.29%)	2 / 25 (8.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Urticaria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry skin	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pruritic	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Micturition urgency	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Proteinuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Dysuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Albuminuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Hypertonic bladder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Osteonecrosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Pain in extremity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 7 (14.29%) 1	10 / 25 (40.00%) 12	1 / 6 (16.67%) 1
Back pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 7 (14.29%) 1	4 / 25 (16.00%) 4	0 / 6 (0.00%) 0
Musculoskeletal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	2 / 25 (8.00%) 2	0 / 6 (0.00%) 0
Flank pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Arthralgia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 7 (0.00%)	3 / 25 (12.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Myalgia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Bone pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in jaw	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscular weakness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dactylitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Viral infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	5 / 25 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Upper respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	2 / 25 (8.00%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Gastroenteritis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 7 (14.29%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0

Body tinea		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Cellulitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Conjunctivitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Acute sinusitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)		0	1	0
Pharyngitis streptococcal		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)		0	1	0
Rhinitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Sinusitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	1 / 25 (4.00%)	0 / 6 (0.00%)
occurrences (all)		0	1	0
Influenza		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Lower respiratory tract infection		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Nasopharyngitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0
Otitis media		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)		0	0	0

Urinary tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COVID-19	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Febrile infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth abscess	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tinea faciei	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sepsis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Impetigo	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatitis A	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 7 (0.00%)	0 / 25 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Oral herpes	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Lip infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Gastroenteritis rotavirus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Tonsillitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory tract infection viral	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Rotavirus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Viral rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
Vitamin D deficiency	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0
Decreased appetite	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
Dehydration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 7 (0.00%) 0	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0
<b>Non-serious adverse events</b>			
Part D: Participants aged 6M to <2 years: Voxelotor Part C: Participants aged 12 to 17 years: Voxelotor 1500 mg Part C: Participants aged 4 to 11 years: Voxelotor 1500 mg			

	1500 mg QD	QD	QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	11 / 11 (100.00%)	46 / 51 (90.20%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign lymph node neoplasm	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Non-cardiac chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	1 / 51 (1.96%)
occurrences (all)	0	1	1
Pyrexia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	4 / 9 (44.44%)	2 / 11 (18.18%)	15 / 51 (29.41%)
occurrences (all)	6	2	27
Pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	4 / 51 (7.84%)
occurrences (all)	0	0	5
Fatigue	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
Chest discomfort	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	1 / 11 (9.09%)	1 / 51 (1.96%)
occurrences (all)	1	1	1
Chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Gait disturbance	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Immune system disorders			



Seasonal allergy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Allergic oedema	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 2
Reproductive system and breast disorders	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Respiratory, thoracic and mediastinal disorders	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Acute chest syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Cough	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	2 / 11 (18.18%) 2	2 / 51 (3.92%) 3
Oropharyngeal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Nasal congestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Epistaxis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	0 / 11 (0.00%) 0	3 / 51 (5.88%) 3
Dyspnoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Rhinorrhoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Upper-airway cough syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Hypoxia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Sinus congestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Paranasal sinus hypersecretion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Obstructive sleep apnoea syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Tonsillar erythema	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Tonsillar hypertrophy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Allergic respiratory symptom			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Stress	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Anxiety	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Insomnia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0

Mental status changes	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Post-traumatic stress disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			1 / 51 (1.96%)
Enuresis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			1 / 51 (1.96%)
Encopresis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			1 / 51 (1.96%)
Investigations			
Transaminases increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			1 / 51 (1.96%)
Bacterial test positive	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Alanine aminotransferase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)
	occurrences (all)	1	0
			2 / 51 (3.92%)
Neutrophil count decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			1 / 51 (1.96%)
Influenza A virus test positive	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			1 / 51 (1.96%)
Haemoglobin decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 9 (11.11%)	1 / 11 (9.09%)
	occurrences (all)	1	1
			0 / 51 (0.00%)
Electrocardiogram QT prolonged	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Breath sounds abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	1	0	2
Blood alkaline phosphatase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Ultrasound head abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Arthropod bite	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Joint injury	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Laceration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Foot fracture	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Epiphyseal fracture	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Sports injury	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
Muscle strain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Foreign body ingestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
Ventricular hypertrophy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Left atrial dilatation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Diastolic dysfunction	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Cardiomegaly	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	9 / 51 (17.65%)
occurrences (all)	0	1	11
Lethargy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Migraine	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Syncope	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Dizziness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Hypersomnia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	5 / 9 (55.56%)	2 / 11 (18.18%)	10 / 51 (19.61%)
occurrences (all)	9	6	19
Anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	1	0	2
Neutropenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	4 / 51 (7.84%)
occurrences (all)	0	0	4

Thrombocytosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	4 / 51 (7.84%)
	0	0	4
Reticulocytopenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
	0	0	0
Splenomegaly	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
	0	0	1
Hypersplenism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
	0	0	0
Hypercoagulation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
	0	0	0
Ear and labyrinth disorders			
Hypoacusis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
	0	0	0
Tinnitus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
	0	0	0
Eye disorders			
Retinopathy sickle cell	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
	0	0	0
Visual impairment	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
	0	1	0
Eye pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%)	1 / 11 (9.09%)	1 / 51 (1.96%)
	0	1	1
Gastrointestinal disorders			

Vomiting	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	5 / 9 (55.56%) 6	1 / 11 (9.09%) 1	15 / 51 (29.41%) 17
Abdominal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	1 / 11 (9.09%) 1	5 / 51 (9.80%) 5
Nausea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	1 / 11 (9.09%) 1	4 / 51 (7.84%) 7
Diarrhoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	2 / 9 (22.22%) 3	1 / 11 (9.09%) 1	10 / 51 (19.61%) 11
Constipation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	0 / 11 (0.00%) 0	2 / 51 (3.92%) 3
Abdominal pain upper	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	4 / 51 (7.84%) 4
Dental caries	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Gastritis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Toothache	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Abdominal distension	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
gastrointestinal disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	1 / 11 (9.09%) 1	0 / 51 (0.00%) 0



Lip blister	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)
	occurrences (all)	1	0
			0 / 51 (0.00%)
Flatulence	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Hepatobiliary disorders			
Cholelithiasis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Ocular icterus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Hypertransaminaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	1
			1 / 51 (1.96%)
Jaundice	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Skin and subcutaneous tissue disorders			
Rash papular	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	1
			1 / 51 (1.96%)
Dermatitis contact	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	1
			1 / 51 (1.96%)
Rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)
	occurrences (all)	1	6
			6 / 51 (11.76%)
Rash generalised	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)
	occurrences (all)	0	0
			0 / 51 (0.00%)
Pruritus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	3
Urticaria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	1	0	1
Dry skin	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Dermatitis allergic	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Rash pruritic	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Micturition urgency	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Proteinuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Dysuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Albuminuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Hypertonic bladder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Osteonecrosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 9 (22.22%)	0 / 11 (0.00%)	7 / 51 (13.73%)
occurrences (all)	2	0	13
Back pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	2 / 11 (18.18%)	3 / 51 (5.88%)
occurrences (all)	0	2	3
Musculoskeletal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Flank pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Arthralgia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	2 / 11 (18.18%)	1 / 51 (1.96%)
occurrences (all)	1	2	1
Myalgia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Bone pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Pain in jaw	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Musculoskeletal chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Muscular weakness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Dactylitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Joint swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Viral infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 9 (22.22%)	0 / 11 (0.00%)	7 / 51 (13.73%)
occurrences (all)	3	0	7
Upper respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 9 (22.22%)	2 / 11 (18.18%)	8 / 51 (15.69%)
occurrences (all)	2	2	11
Gastroenteritis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Body tinea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Cellulitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
Acute sinusitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Pharyngitis streptococcal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1

Rhinitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Sinusitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	0 / 51 (0.00%) 0
Influenza	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	0 / 11 (0.00%) 0	3 / 51 (5.88%) 3
Lower respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	2 / 11 (18.18%) 2	0 / 51 (0.00%) 0
Nasopharyngitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	2 / 11 (18.18%) 2	0 / 51 (0.00%) 0
Otitis media	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	2 / 51 (3.92%) 2
Urinary tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	1 / 9 (11.11%) 1	0 / 11 (0.00%) 0	2 / 51 (3.92%) 2
COVID-19	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Febrile infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Tooth abscess	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1
Viral upper respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 9 (0.00%) 0	0 / 11 (0.00%) 0	1 / 51 (1.96%) 1

Tinea faciei		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)		0	0	1
Sepsis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)		0	0	1
Impetigo		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)		0	0	1
Hepatitis A		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)		0	0	1
Pneumonia		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		1	0	0
Respiratory syncytial virus infection		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		0	0	0
Oral herpes		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		2	0	0
Lip infection		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		1	0	0
Gastroenteritis rotavirus		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		1	0	0
Tonsillitis		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		0	0	0
Respiratory tract infection viral		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed		1 / 9 (11.11%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)		1	0	0

Rotavirus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Viral rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin D deficiency	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Decreased appetite	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Dehydration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1

<b>Non-serious adverse events</b>	Part D: Participants aged 2 to <4 years: Voxelotor 1500 mg	Part B: Voxelotor 1500 mg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 23 (91.30%)	15 / 15 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
Benign lymph node neoplasm			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Non-cardiac chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Pyrexia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	8 / 23 (34.78%)	2 / 15 (13.33%)	
occurrences (all)	12	4	
Pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Fatigue	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chest discomfort	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Peripheral swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gait disturbance	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Seasonal allergy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Allergic oedema	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Priapism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Acute chest syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Cough	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		



subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Oropharyngeal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Nasal congestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Epistaxis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Dyspnoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Upper-airway cough syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypoxia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Sinus congestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Paranasal sinus hypersecretion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Obstructive sleep apnoea syndrome	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Tonsillar erythema	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Tonsillar hypertrophy	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Allergic respiratory symptom			
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Psychiatric disorders			
Stress	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 15 (6.67%) 1	
Anxiety	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 15 (6.67%) 1	
Insomnia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Mental status changes	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 15 (6.67%) 1	
Post-traumatic stress disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Enuresis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Encopresis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Investigations			
Transaminases increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Bacterial test positive	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Influenza A virus test positive	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Haemoglobin decreased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Breath sounds abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Ultrasound head abnormal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

	1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Arthropod bite	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Joint injury	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Laceration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Foot fracture	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Epiphyseal fracture	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Sports injury	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Muscle strain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Foreign body ingestion	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

<p>Tachycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ventricular hypertrophy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Left atrial dilatation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diastolic dysfunction</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cardiomegaly</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
<p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Lethargy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Migraine</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Syncope</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Depressed level of consciousness</p>	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	4 / 15 (26.67%)	
	0	10	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	0 / 23 (0.00%)	0 / 15 (0.00%)	
	0	0	

subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hypersomnia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	10 / 23 (43.48%)	3 / 15 (20.00%)	
occurrences (all)	14	6	
Anaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Neutropenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Thrombocytopenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Thrombocytosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Reticulocytopenia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Splenomegaly	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hypersplenism	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hypercoagulation	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Ear and labyrinth disorders			
	Hypoacusis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
	Tinnitus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
Eye disorders			
	Retinopathy sickle cell	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	2
	Visual impairment	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Eye pain		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Gastrointestinal disorders			
	Vomiting	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	2 / 23 (8.70%)	2 / 15 (13.33%)
	occurrences (all)	2	2
	Abdominal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	1 / 23 (4.35%)	3 / 15 (20.00%)
	occurrences (all)	1	3
	Nausea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	1 / 23 (4.35%)	3 / 15 (20.00%)
	occurrences (all)	1	5
	Diarrhoea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	3 / 23 (13.04%)	2 / 15 (13.33%)
	occurrences (all)	3	3
Constipation		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)
	occurrences (all)	2	0
Abdominal pain upper		Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	

subjects affected / exposed	2 / 23 (8.70%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Dental caries	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Gastritis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Toothache	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Abdominal distension	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
gastrointestinal disorder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Lip blister	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Cholelithiasis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ocular icterus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hypertransaminasaemia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	



Jaundice	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)
	occurrences (all)	1	0
Skin and subcutaneous tissue disorders			
Rash papular	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Dermatitis contact	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)
	occurrences (all)	2	1
Rash generalised	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
Pruritus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	2 / 15 (13.33%)
	occurrences (all)	0	4
Urticaria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Rash maculo-papular	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Dry skin	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Dermatitis allergic	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Rash pruritic	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Renal and urinary disorders			
Micturition urgency	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Proteinuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Dysuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Albuminuria	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Hypertonic bladder	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	0 / 15 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Pain in extremity	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 6	3 / 15 (20.00%) 8	
Back pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	4 / 15 (26.67%) 4	
Musculoskeletal pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0	
Flank pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		

subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Arthralgia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	9	
Myalgia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Bone pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pain in jaw	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Muscular weakness	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Dactylitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Joint swelling	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Viral infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
subjects affected / exposed	7 / 23 (30.43%)	2 / 15 (13.33%)	
occurrences (all)	7	2	

Gastroenteritis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)
	occurrences (all)	1	0
Body tinea	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
Cellulitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
Conjunctivitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
Acute sinusitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Pharyngitis streptococcal	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Rhinitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)
	occurrences (all)	0	1
Sinusitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Influenza	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)
	occurrences (all)	1	0
Lower respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)
	occurrences (all)	0	0
Nasopharyngitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms		
	subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)
	occurrences (all)	1	0

Otitis media	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	1 / 23 (4.35%)	0 / 15 (0.00%)
subjects affected / exposed	1	0
occurrences (all)		
Urinary tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
COVID-19	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	4 / 23 (17.39%)	0 / 15 (0.00%)
subjects affected / exposed	4	0
occurrences (all)		
Febrile infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Tooth abscess	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	1 / 23 (4.35%)	0 / 15 (0.00%)
subjects affected / exposed	1	0
occurrences (all)		
Viral upper respiratory tract infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	1 / 23 (4.35%)	0 / 15 (0.00%)
subjects affected / exposed	1	0
occurrences (all)		
Tinea faciei	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Sepsis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Impetigo	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Hepatitis A	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Pneumonia	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		

Respiratory syncytial virus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	1 / 23 (4.35%)	0 / 15 (0.00%)
subjects affected / exposed	1	0
occurrences (all)		
Oral herpes	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Lip infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Gastroenteritis rotavirus	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Tonsillitis	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	2 / 23 (8.70%)	0 / 15 (0.00%)
subjects affected / exposed	2	0
occurrences (all)		
Respiratory tract infection viral	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	2 / 23 (8.70%)	0 / 15 (0.00%)
subjects affected / exposed	3	0
occurrences (all)		
Rotavirus infection	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	1 / 23 (4.35%)	0 / 15 (0.00%)
subjects affected / exposed	1	0
occurrences (all)		
Viral rash	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	1 / 23 (4.35%)	0 / 15 (0.00%)
subjects affected / exposed	1	0
occurrences (all)		
Metabolism and nutrition disorders		
	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
Vitamin D deficiency	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Decreased appetite	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	
	0 / 23 (0.00%)	0 / 15 (0.00%)
subjects affected / exposed	0	0
occurrences (all)		
Dehydration	Additional description: MedDRA v19.1 for Part A and Part B arms, MedDRA v25.1 for Part C arms and MedDRA v26.0 for Part D arms	

subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2016	Amendment 1: Modified restrictions regarding concomitant medications to reflect new data regarding the potential of voxelotor to interact with cytochrome P (CYP) substrates.
10 November 2016	Amendment 2: In Part B, increased duration of study drug dosing to 24 weeks. In Part B, revised voxelotor dose groups to 900 mg and 1500 mg. Updated objectives and endpoints of the study to reflect the revisions to Part B (eg, increased dosing period and changes in doses).
06 March 2017	Amendment 3: Added an independent Drug Safety Monitoring Board (DSMB) to monitor the safety and conduct of the study. Added a taste and palatability questionnaire to evaluate the pediatric participants taste and palatability experience after taking study drug. Added a study drug formulation that was the granulation from the voxelotor common blend capsules (to be mixed with food by the caregiver and administered to participants aged 6–11 years).
09 June 2017	Amendment 4: For Part B, revised the age distribution of the sample size (approximately, 36 pediatric participants). For Part B, increased the duration of the Screening Period from 28 days to 35 days to allow for greater visit scheduling flexibility for parents and children. For Part B, revised the dose-modification guidelines and additional actions for liver function test (LFT) elevations of alanine aminotransferase (ALT) $\geq 5 \times$ upper limit of normal (ULN) and $< 10 \times$ ULN.
14 June 2018	Amendment 5: Added Part C to the study (including objectives, endpoints, additional participants, additional study entry criteria, Schedule of Assessments, analysis methods) to assess the safety, tolerability, PK, hematologic response, and effect on TCD flow velocity of voxelotor in participants with SCD aged 4 to 17 years. Added the dispersible tablet formulation (50, 100, and/or 300 mg) of voxelotor for oral administration to subjects in Part C. Increased the number of clinical sites participating in the study to approximately 25 to allow for enrollment of participants in Part C. Added Part C to the ongoing safety and data review performed by the DSMB. Updated the dose-modification guidelines for participants aged 12 to 17 years and added dose-modification tables for participants aged 4 to 11 years in Part C. Removed the requirement that participants avoid a high-fat meal within 4 hours of voxelotor administration to align with the ongoing Phase 3 study GBT440-031. Updated fertility/contraception requirements based on available nonclinical data indicating that voxelotor administration was associated with a low risk of genotoxic effects and had no effects on embryo-fetal development or fertility.
15 November 2019	Amendment 6: Added Part D to the study (including objectives, endpoints, additional subjects, additional study entry criteria, Schedule of Assessments, analysis methods) to assess the safety, tolerability, PK, and hematologic response of voxelotor 1500-mg equivalent in approximately 30 pediatric participants aged 9 months to $< 4$ years. Updated the summary of known and potential risks and benefits of voxelotor and also the risk assessment for voxelotor. Updated restrictions regarding concomitant medications to align with current clinical pharmacological data for voxelotor. For Part C, removed voxelotor 50 mg dispersible tablets and added voxelotor powder for oral suspension formulation. Updated PK-related secondary endpoint (Part C) and PK analysis, and included an additional Hb-related secondary endpoint.



28 April 2021	Amendment 7: For Part C, added 2 new secondary objectives evaluating the proportion of participants with normal TCD flow velocity and the effect of voxelotor on the incidence of stroke and VOC. For Part D, changed the range of pediatric participants being evaluated from 9 months to < 4 years of age to 6 months to < 4 years of age. For Part D, added a new secondary objective evaluating the effect of voxelotor on the incidence of stroke and VOC in pediatric participants with SCD. Added a new exclusion criterion for active symptomatic COVID-19 infection.
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Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported