



Clinical trial results:

An Open-Label Extension Study of Voxelotor Administered Orally to Participants with Sickle Cell Disease who Have Participated in Voxelotor Clinical Trials

Summary

EudraCT number	2019-003144-76
Trial protocol	GB
Global end of trial date	31 October 2024

Results information

Result version number	v1 (current)
This version publication date	15 November 2025
First version publication date	15 November 2025

Trial information

Trial identification

Sponsor protocol code	C5341023
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04188509
WHO universal trial number (UTN)	-
Other trial identifiers	Other Study ID: GBT440-038

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Boulevard East, New York, United States, NY 10001-2192
Public contact	Pfizer ClinicalTrials.govCall Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.govCall Center, Pfizer Inc., 001 8007181021, 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	05 September 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 October 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this open-label extension (OLE) study is to assess the safety of, and sickle cell disease (SCD)-related complications with, long-term treatment with voxelotor in participants who have completed treatment in a global blood therapeutics (GBT)-sponsored voxelotor clinical study, based on the following parameters: adverse events (AEs), clinical laboratory tests, physical examinations (PEs), and other clinical measures and frequency of SCD-related complications.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Egypt: 9
Country: Number of subjects enrolled	Lebanon: 19
Country: Number of subjects enrolled	Nigeria: 99
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 29
Worldwide total number of subjects	162
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)	130

Adolescents (12-17 years)	22
Adults (18-64 years)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 162 participants who had previously completed following studies: GBT440-032 (NCT04218084) who received placebo, and GBT440-007 (NCT02850406), GBT440-032 (NCT04218084) or GBT440-042 (NCT05561140) who received voxelotor were enrolled in current study GBT440-038 (NCT04188509). All participants enrolled in this study received voxelotor.

Pre-assignment

Screening details:

A total of 162 participants were enrolled and randomized in this study.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	Voxelotor
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Arm description:

Participants aged ≥ 12 years received voxelotor 1500 milligrams (mg) once daily (QD) tablets. Participants aged < 12 years received a voxelotor dose based on their body weight to provide exposure corresponding to the adult dose of 1500 mg QD as powder for oral suspension or dispersible tablet or modified dispersible tablet. Participants received study drug as long they continued to receive clinical benefit that outweighed risk as determined by the investigator and/or until the participant had access to voxelotor from an alternative source.

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

Dosage and administration details:

Voxelotor 1500 mg, 400 mg, 600 mg, 900 mg QD tablets for participants according to their body weight.

Number of subjects in period 1	Voxelotor
Started	162
Completed	25
Not completed	137
Consent withdrawn by subject	1
Physician decision	1
Adverse event, non-fatal	2
Non-compliance	3
Unspecified	2

Lost to follow-up	1
Sponsor decision	127

Baseline characteristics

Reporting groups

Reporting group title	Voxelotor
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Reporting group description:

Participants aged ≥ 12 years received voxelotor 1500 milligrams (mg) once daily (QD) tablets. Participants aged < 12 years received a voxelotor dose based on their body weight to provide exposure corresponding to the adult dose of 1500 mg QD as powder for oral suspension or dispersible tablet or modified dispersible tablet. Participants received study drug as long they continued to receive clinical benefit that outweighed risk as determined by the investigator and/or until the participant had access to voxelotor from an alternative source.

Reporting group values	Voxelotor	Total	
Number of subjects	162	162	
Age Categorical Units: Subjects			
Age continuous Units: Years arithmetic mean standard deviation	9.2 ± 5.68	-	
Gender categorical Units: Participants			
Female	75	75	
Male	87	87	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	161	161	
Unknown or Not Reported	0	0	
Race Units: Subjects			
African	94	94	
Arab	2	2	
Black or African American	40	40	
Middle Eastern or North African	9	9	
White	10	10	
Multi-Racial	7	7	

End points

End points reporting groups

Reporting group title	Voxelotor
Reporting group description: Participants aged ≥ 12 years received voxelotor 1500 milligrams (mg) once daily (QD) tablets. Participants aged < 12 years received a voxelotor dose based on their body weight to provide exposure corresponding to the adult dose of 1500 mg QD as powder for oral suspension or dispersible tablet or modified dispersible tablet. Participants received study drug as long they continued to receive clinical benefit that outweighed risk as determined by the investigator and/or until the participant had access to voxelotor from an alternative source.	

Primary: Number of Participants With Treatment Emergent Adverse Events (AEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (AEs) ^[1]
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End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered to be drug related. A treatment emergent AE was defined as an AE with an onset date on or after the date of informed consent until 28 days after discontinuation of drug. AEs included both serious AEs (SAEs) and all non-SAEs. An SAE was an AE or suspected adverse reaction that, at any dose, in the view of the either the investigator or sponsor, resulted in any of the following outcomes: death, was life-threatening, resulted in persistent disability/incapacity; constituted a congenital anomaly/birth defect; was important medical event; required inpatient hospitalization or prolongation of existing hospitalization.

End point type	Primary
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End point timeframe:

From date of informed consent until 28 days after last dose of study drug (maximum up to 4.31 years)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	Voxelotor			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Participants	105			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Sickle Cell Disease (SCD) Related TEAEs and SAEs

End point title	Number of Participants With Sickle Cell Disease (SCD) Related TEAEs and SAEs ^[2]
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End point description:

SCD-related AEs were common complications associated with the study participant's SCD and were not considered to be related to voxelotor unless judged by the investigator to have worsened in severity and/or frequency or changed in nature during the study. SCD-related complications included the following: sickle cell anemia with crisis, acute chest syndrome (ACS), pneumonia, priapism, and osteonecrosis. A treatment emergent AE was defined as an AE with an onset date on or after the date of

informed consent until 28 days after discontinuation of drug. An SAE was an AE or suspected adverse reaction that, at any dose, in the view of either the investigator or sponsor, resulted in any of the following outcomes: death, was life-threatening, resulted in persistent disability/incapacity; constituted a congenital anomaly/birth defect; was important medical event; required inpatient hospitalization or prolongation of existing hospitalization.

End point type	Primary
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End point timeframe:

From date of informed consent until 28 days after last dose of study drug (maximum up to 4.31 years)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	Voxelotor			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Participants				
SCD related treatment emergent AE	60			
SCD Related SAE	43			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With SAEs

End point title	Number of Participants With SAEs ^[3]
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End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered to be drug related. An SAE was an AE or suspected adverse reaction that, at any dose, in the view of the either the investigator or sponsor, resulted in any of the following outcomes: death, was life-threatening, resulted in persistent disability/incapacity; constituted a congenital anomaly/birth defect; was important medical event; required inpatient hospitalization or prolongation of existing hospitalization. The safety population included all participants who received at least 1 dose of study drug.

End point type	Primary
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End point timeframe:

From date of informed consent until 28 days after last dose of study drug (maximum up to 4.31 years)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	Voxelotor			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Participants	53			

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of informed consent until 28 days after last dose of study drug (maximum up to 4.31 years)

Adverse event reporting additional description:

Same events may appear as both SAE and non-SAE, but what is presented are distinct events. An event may be categorized as serious in one participant and as non-serious in another, or one participant may have experienced both serious and non-serious event during study. Safety population: all participants who received at least one dose of study drug.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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Reporting groups

Reporting group title	Voxelotor
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Reporting group description:

Participants aged ≥ 12 years received voxelotor 1500 mg QD tablets. Participants aged < 12 years received a voxelotor dose based on their body weight to provide exposure corresponding to the adult dose of 1500 mg QD as powder for oral suspension or dispersible tablet or modified dispersible tablet. Participants received study drug as long they continued to receive clinical benefit that outweighed risk as determined by the investigator and/or until the participant had access to voxelotor from an alternative source.

Serious adverse events	Voxelotor		
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 162 (32.72%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			

subjects affected / exposed	2 / 162 (1.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	8 / 162 (4.94%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Priapism			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Acute chest syndrome			
subjects affected / exposed	15 / 162 (9.26%)		
occurrences causally related to treatment / all	0 / 20		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paranasal cyst			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Liver function test increased			

subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Acute haemolytic transfusion reaction			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Congenital, familial and genetic disorders			
Urethral valves			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haemolysis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Splenic sequestration crisis			
subjects affected / exposed	5 / 162 (3.09%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	16 / 162 (9.88%)		
occurrences causally related to treatment / all	0 / 41		
deaths causally related to treatment / all	0 / 0		
Sickle cell anaemia with crisis			

subjects affected / exposed	35 / 162 (21.60%)		
occurrences causally related to treatment / all	2 / 75		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bone pain			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 162 (1.85%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 162 (1.85%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	6 / 162 (3.70%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Malaria			
subjects affected / exposed	8 / 162 (4.94%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound sepsis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Voxelotor		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 162 (57.41%)		
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Surgical and medical procedures			
Splenectomy			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
General disorders and administration site conditions			

Non-cardiac chest pain subjects affected / exposed occurrences (all)	3 / 162 (1.85%) 7		
Decreased activity subjects affected / exposed occurrences (all)	1 / 162 (0.62%) 1		
Swelling face subjects affected / exposed occurrences (all)	1 / 162 (0.62%) 1		
Pain subjects affected / exposed occurrences (all)	1 / 162 (0.62%) 1		
Pyrexia subjects affected / exposed occurrences (all)	20 / 162 (12.35%) 32		
Reproductive system and breast disorders Painful erection subjects affected / exposed occurrences (all)	1 / 162 (0.62%) 1		
Priapism subjects affected / exposed occurrences (all)	1 / 162 (0.62%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	5 / 162 (3.09%) 5		
Oropharyngeal pain subjects affected / exposed occurrences (all)	4 / 162 (2.47%) 5		
Tonsillar hypertrophy subjects affected / exposed occurrences (all)	2 / 162 (1.23%) 2		
Acute chest syndrome subjects affected / exposed occurrences (all)	1 / 162 (0.62%) 1		
Epistaxis			

subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Investigations			
Platelet count increased			
subjects affected / exposed	5 / 162 (3.09%)		
occurrences (all)	5		
Eosinophil count increased			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	4		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Red cell distribution width abnormal			
subjects affected / exposed	3 / 162 (1.85%)		
occurrences (all)	3		
Blood calcium decreased			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Blood urea decreased			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Haemoglobin decreased			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Platelet count decreased			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		

Alanine aminotransferase increased			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Bilirubin conjugated increased			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Mean cell volume decreased			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Arthropod bite			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Head injury			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Lip injury			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Traumatic pain			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Fall			

subjects affected / exposed occurrences (all)	2 / 162 (1.23%) 2		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 162 (3.70%)		
occurrences (all)	9		
Cluster headache			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis			
subjects affected / exposed	27 / 162 (16.67%)		
occurrences (all)	53		
Anaemia			
subjects affected / exposed	9 / 162 (5.56%)		
occurrences (all)	12		
Thrombocytosis			
subjects affected / exposed	6 / 162 (3.70%)		
occurrences (all)	6		
Neutropenia			
subjects affected / exposed	3 / 162 (1.85%)		
occurrences (all)	3		
Splenic sequestration crisis			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	4		
Thrombocytopenia			

subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Cytopenia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Hypersplenism			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Macrocytosis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Splenomegaly			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Cholesteatoma			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Eye disorders			
Vernal keratoconjunctivitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	3 / 162 (1.85%)		
occurrences (all)	5		
Salivary hypersecretion			

subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Anal pruritus			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	6 / 162 (3.70%)		
occurrences (all)	11		
Vomiting			
subjects affected / exposed	6 / 162 (3.70%)		
occurrences (all)	6		
Toothache			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Peptic ulcer			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Hepatosplenomegaly			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Pityriasis rosea			

subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	2		
Dermatitis contact			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Renal and urinary disorders			
Hypertonic bladder			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	6 / 162 (3.70%)		
occurrences (all)	8		
Arthralgia			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	5		
Bone pain			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Osteonecrosis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Spinal osteoarthritis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Infections and infestations			

Viral upper respiratory tract infection			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	3 / 162 (1.85%)		
occurrences (all)	6		
Viral infection			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	5		
Tonsillitis			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	7		
Pneumonia			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	4		
COVID-19			
subjects affected / exposed	4 / 162 (2.47%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	5 / 162 (3.09%)		
occurrences (all)	6		
Gastroenteritis			
subjects affected / exposed	5 / 162 (3.09%)		
occurrences (all)	5		
Malaria			
subjects affected / exposed	10 / 162 (6.17%)		
occurrences (all)	11		
Upper respiratory tract infection			
subjects affected / exposed	13 / 162 (8.02%)		
occurrences (all)	25		
Varicella			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		

Staphylococcal bacteraemia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Skin candida			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Sepsis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Pharyngotonsillitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Periorbital cellulitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Mumps			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		

Gastroenteritis viral			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Enterovirus infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Diarrhoea infectious			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Croup infectious			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Coronavirus infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Bronchitis viral			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Body tinea			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Adenovirus infection			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	9 / 162 (5.56%)		
occurrences (all)	9		
Hypocalcaemia			
subjects affected / exposed	2 / 162 (1.23%)		
occurrences (all)	2		
Abnormal loss of weight			

subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2020	Clarified reporting requirements for AEs; only serious adverse events must be reported within 24 hours, as already indicated in the protocol.
13 September 2021	Added specific guidance to the investigator on appropriate dose modifications to manage adverse events, as the safety profile was established based on a Phase 3 study, only abnormal laboratory values that are clinically significant will be collected and summarized.
10 August 2022	Removed "hemolytic anemia" and added "to significantly increase Hb, improve anaemia, and reduce clinical measures of hemolysis" to the justification for dose selection. Changed the dose reduction 2 new dose for weight 5 to less than 10 kg from "not applicable" to "200 mg".
15 June 2023	Provided a broader definition of SCD-related AEs for safety analyses, provided guidance for investigators on collection of any adverse events potentially associated with the modified dose of dispersible tablets.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported