Clinical trial results:
A Phase 2a, Double-blind, Randomised, Placebo-controlled, Efficacy, and Safety Study of Multiple Doses of VIT-2763 in Subjects With Sickle Cell Disease (ViSion Serenity)

Summary

EudraCT number	2020-005072-34
Trial protocol	GR
Global end of trial date	07 March 2024

Results information

Result version number	v1 (current)
This version publication date	12 February 2025
First version publication date	12 February 2025

Trial information

Trial identification

Sponsor protocol code	VIT-2763-SCD-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04817670
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 147878

Notes:

Sponsors

Sponsor organisation name	Vifor (International) Inc.
Sponsor organisation address	Rechenstrasse 37, St. Gallen, Switzerland, CH-9014
Public contact	Study Director, CSL Behring LLC, +1 610 878 4000, clinicaltrials@cslbehring.com
Scientific contact	Study Director, CSL Behring LLC, +1 610 878 4000, clinicaltrials@cslbehring.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to explore the effect of VIT-2763 on markers of haemolysis.

Protection of trial subjects:

This study was carried out in accordance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, the ethical principles that have their origin in the Declaration of Helsinki, all applicable national and local regulations, and standard operating procedures for clinical research and development at Vifor. The study protocol and all amendments were approved by the Independent Ethics Committee (IEC) / Institutional Review Board (IRB) of the participating center. Before any protocol-specific procedures were carried out, participants were informed, in an understandable form, about the nature, scope, and possible consequences of the study. Participant informed consent was obtained and documented according to the provisions of ICH GCP and applicable regulatory requirements. Written informed consent was provided by each participant before any protocol-specific procedures were carried out.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2021
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: 10
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Greece: 2
Worldwide total number of subjects	25
EEA total number of subjects	3

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 22 sites initiated for this study in 5 countries (The United Kingdom, Lebanon, Greece, the United States, and France).

Pre-assignment

Screening details:

A total of 46 participants were screened in this study, of which 28 were screen failures. Out of these 28 participants, 9 were rescreened, and 7 were found eligible for the study. 25 participants were enrolled in the study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)

Arm description:

Participants received VIT-2763 60 milligrams (mg) (2 x 30 mg capsules), orally, twice daily (BID) for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	VIT-2763
Investigational medicinal product code	VIT-2763
Other name	Vamifeport
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

VIT-2763 capsule for oral administration.

Arm title	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)

Arm description:

Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, BID for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	VIT-2763
Investigational medicinal product code	VIT-2763
Other name	Vamifeport
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

VIT-2763 capsule for oral administration.

Arm title	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)

Arm description:

Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, three times daily (TID) for 8 weeks.

Arm type	Experimental

Investigational medicinal product name	VIT-2763
Investigational medicinal product code	VIT-2763
Other name	Vamifeport
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

VIT-2763 capsule for oral administration.

Arm title	Cohort 4: Placebo

Arm description:

Participants received placebo capsules, orally, BID or TID for 8 weeks.

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

Dosage and administration details:

Placebo capsule for oral administration.

Arm title	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)

Arm description:

One participant received VIT-2763 30 mg, orally, BID for 8 weeks under Protocol Version 2.0. However, after the implementation of Protocol Version 3.0 and higher, this participant was excluded from the efficacy analysis and only safety data were reported (as planned).

Arm type	Experimental
Investigational medicinal product name	VIT-2763
Investigational medicinal product code	VIT-2763
Other name	Vamifeport
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

VIT-2763 capsule for oral administration.

Number of subjects in period 1	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)
Started	6	6	6
Intent-to-treat (ITT) Population	6	6	6
Completed	5	6	5
Not completed	1	0	1
Lost to follow-up	-	-	1
Withdrawal by subject	1	-	-

Number of subjects in period 1	Cohort 4: Placebo	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)
Started	6	1
Intent-to-treat (ITT) Population	6	0 [1]

Completed	6	1
Not completed	0	0
Lost to follow-up	-	-
Withdrawal by subject	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: One participant in Cohort 2a arm was enrolled under Protocol Version 2.0. However, after the implementation of Protocol Version 3.0 and higher, this participant was excluded from the efficacy analysis and only safety data were reported (as planned).

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)
Reporting group description:	
Participants received VIT-2763 60 milligrams (mg) (2 x 30 mg capsules), orally, twice daily (BID) for 8 weeks.	
Reporting group title	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)
Reporting group description:	
Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, BID for 8 weeks.	
Reporting group title	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)
Reporting group description:	
Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, three times daily (TID) for 8 weeks.	
Reporting group title	Cohort 4: Placebo
Reporting group description:	
Participants received placebo capsules, orally, BID or TID for 8 weeks.	
Reporting group title	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)
Reporting group description:	
One participant received VIT-2763 30 mg, orally, BID for 8 weeks under Protocol Version 2.0. However, after the implementation of Protocol Version 3.0 and higher, this participant was excluded from the efficacy analysis and only safety data were reported (as planned).	

Reporting group values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)
Number of subjects	6	6	6
Age categorical			
Units: Subjects			
Age continuous			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: years			
arithmetic mean	30.2	36.0	29.3
standard deviation	± 7.41	± 11.87	± 9.48
Gender categorical			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: Subjects			
Female	4	3	3
Male	2	3	3
Not disclosed	0	0	0
Ethnicity			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	6	5
Unknown or Not Reported	1	0	1
Not disclosed	0	0	0
Race			

Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	3	3
White	4	3	2
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Not disclosed	0	0	0

Reporting group values	Cohort 4: Placebo	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)	Total
Number of subjects	6	1	25
Age categorical			
Units: Subjects			
Age continuous			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: years			
arithmetic mean	25.3	0.00	
standard deviation	± 7.17	± 0.00	-
Gender categorical			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: Subjects			
Female	3	0	13
Male	3	0	11
Not disclosed	0	1	1
Ethnicity			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	0	22
Unknown or Not Reported	0	0	2
Not disclosed	0	1	1
Race			
Data for Cohort 2a not reported here due to concerns regarding participant privacy as there was only 1 participant in Cohort 2a arm.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	0	12
White	2	0	11
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Not disclosed	0	1	1

End points

End points reporting groups

Reporting group title	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)
Reporting group description:	
Participants received VIT-2763 60 milligrams (mg) (2 x 30 mg capsules), orally, twice daily (BID) for 8 weeks.	
Reporting group title	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)
Reporting group description:	
Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, BID for 8 weeks.	
Reporting group title	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)
Reporting group description:	
Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, three times daily (TID) for 8 weeks.	
Reporting group title	Cohort 4: Placebo
Reporting group description:	
Participants received placebo capsules, orally, BID or TID for 8 weeks.	
Reporting group title	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)
Reporting group description:	
One participant received VIT-2763 30 mg, orally, BID for 8 weeks under Protocol Version 2.0. However, after the implementation of Protocol Version 3.0 and higher, this participant was excluded from the efficacy analysis and only safety data were reported (as planned).	

Primary: Mean Change From Baseline in Haemolysis Marker (Indirect Bilirubin)

End point title	Mean Change From Baseline in Haemolysis Marker (Indirect Bilirubin)[1][2]
End point description:	
Mean change from baseline in haemolysis markers was measured by reduction of indirect bilirubin. This analysis was performed on intent-to-treat (ITT) population. The ITT population consisted of all participants who were randomly assigned to a treatment group under Protocol Version 3.0 or higher. Here, the 'overall number of participants analyzed' (N) signifies the number of participants with evaluable data for this outcome measure. The 'number analyzed' (n) signifies the number of participants with evaluable data for each specified timepoint.	
End point type	Primary
End point timeframe:	
Baseline and after 8 weeks of treatment	

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: As the endpoint was descriptive, no statistical hypothesis testing was planned or conducted.
[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: Data for all applicable arms is reported for this endpoint (except Cohort2a after implementation of Protocol Version 3 and higher [as planned]).

End point values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	6
Units: micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				

Baseline (n=5,5,5,6)	24.0 (± 13.51)	56.4 (± 43.71)	44.0 (± 24.48)	31.2 (± 12.95)
Change at 8 weeks (n=4,4,4,5)	-4.0 (± 4.69)	-5.8 (± 11.35)	-21.8 (± 11.62)	0.6 (± 7.30)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Haemolysis Marker (Direct and Total Bilirubin)

End point title	Mean Change From Baseline in Haemolysis Marker (Direct and Total Bilirubin)[3]

End point description:

Mean change from Baseline in haemolysis markers was measured by direct and total bilirubin. This analysis was performed on ITT population. The ITT population consisted of all participants who were randomly assigned to a treatment group under Protocol Version 3.0 or higher. Here, the 'overall number of participants analyzed' (N) signifies the number of participants with evaluable data for this outcome measure. The 'number analyzed' (n) signifies the number of participants with evaluable data for each specified category.

End point type	Secondary

End point timeframe:

Baseline and after 8 weeks of treatment

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for all applicable arms is reported for this endpoint (except Cohort2a after implementation of Protocol Version 3 and higher [as planned]).

End point values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	6
Units: umol/L				
arithmetic mean (standard deviation)				
Direct Bilirubin (n=4,4,4,5)	-0.5 (± 1.29)	-2.0 (± 2.83)	-2.5 (± 7.05)	-0.4 (± 1.52)
Total Bilirubin (n=5,6,5,6)	-4.2 (± 4.76)	-13.2 (± 16.57)	-26.0 (± 16.00)	-0.2 (± 7.08)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Haemolysis Marker (Lactate Dehydrogenase)

End point title	Mean Change From Baseline in Haemolysis Marker (Lactate Dehydrogenase)[4]

End point description:

Mean change from Baseline in haemolysis markers was measured by lactate dehydrogenase. This analysis was performed on ITT population. The ITT population consisted of all participants who were randomly assigned to a treatment group under Protocol Version 3.0 or higher. Here, the 'overall number

of participants analyzed' (N) signifies the number of participants with evaluable data for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and after 8 weeks of treatment

Notes:

[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: Data for all applicable arms is reported for this endpoint (except Cohort2a after implementation of Protocol Version 3 and higher [as planned]).

End point values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	5
Units: units per liter (U/L)				
arithmetic mean (standard deviation)	-45.8 (± 47.56)	-24.0 (± 6.08)	7.7 (± 197.50)	47.8 (± 60.06)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Haemolysis Marker (Potassium)

End point title	Mean Change From Baseline in Haemolysis Marker

End point description:

Mean change from Baseline in haemolysis markers was measured by potassium. This analysis was performed on ITT population. The ITT population consisted of all participants who were randomly assigned to a treatment group under Protocol Version 3.0 or higher. Here, the 'overall number of participants analyzed' (N) signifies the number of participants with evaluable data for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and after 8 weeks of treatment

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for all applicable arms is reported for this endpoint (except Cohort2a after implementation of Protocol Version 3 and higher [as planned]).

End point values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	6
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.08 (± 0.396)	0.08 (± 0.192)	-0.22 (± 0.319)	-0.05 (± 0.295)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Haemolysis Marker (Hemoglobin and Haptoglobin)

End point title	Mean Change From Baseline in Haemolysis Marker (Hemoglobin and Haptoglobin)[6]

End point description:

Mean change from Baseline in haemolysis markers was measured by hemoglobin and haptoglobin. This analysis was performed on ITT population. The ITT population consisted of all participants who were randomly assigned to a treatment group under Protocol Version 3.0 or higher. Here, the 'overall number of participants analyzed' (N) signifies the number of participants with evaluable data for this outcome measure. The 'number analyzed' (n) signifies the number of participants with evaluable data for each specified category.

End point type	Secondary

End point timeframe:

Baseline and after 8 weeks of treatment

Notes:

[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: Data for all applicable arms is reported for this endpoint (except Cohort2a after implementation of Protocol Version 3 and higher [as planned]).

End point values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	5	6
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Hemoglobin (n=5,6,4,6)	-3.400 (± 1.4748)	-2.067 (± 5.5142)	-1.575 (± 8.4017)	2.733 (± 9.9933)
Haptoglobin (n=5,6,5,6)	0.102 (± 0.2281)	-0.012 (± 0.0286)	0.528 (± 0.8312)	0.000 (± 0.0000)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs), TEAEs Related to IMP and by Severity of TEAEs

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs), TEAEs Related to IMP and by Severity of TEAEs

End point description:

TEAEs were defined as adverse events (AEs) with an onset date later or on the same date as the first investigational medicinal product (IMP) intake. The severity grading was determined according to the Common Terminology Criteria for AEs, where the Common Terminology Criteria grades relate to severity as follows: Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening and Grade 5: Death. Analysis was performed on the safety set. The safety set consists of all randomized participants (under Protocol Version 3.0 or higher) who had taken at least one dose of IMP. The participants in the safety set were analyzed based on the treatment they received, regardless of randomization. Data are separately reported for the one participant in the Cohort 2a arm (randomized under Protocol Version 2.0).

End point type	Secondary

End point timeframe:

From first dose of study drug up to 12 weeks

End point values	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: participants				
Any TEAEs	4	4	5	5
TEAEs related to IMP	0	0	0	1
TEAEs with severity: Mild	0	3	2	3
TEAEs with severity: Moderate	3	1	1	2
TEAEs with severity: Severe	1	0	2	0
TEAEs with severity: Life threatening	0	0	0	0
TEAEs with severity: Death	0	0	0	0

End point values	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: participants				
Any TEAEs	1			
TEAEs related to IMP	0			
TEAEs with severity: Mild	1			
TEAEs with severity: Moderate	1			
TEAEs with severity: Severe	0			
TEAEs with severity: Life threatening	0			
TEAEs with severity: Death	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug up to 12 weeks

Adverse event reporting additional description:

Safety set consists of all randomized participants (under Protocol Version 3.0 or higher) who had taken at least one dose of IMP. Participants in safety set were analyzed based on the treatment they received, regardless of randomization. Data are separately reported for the 1 participant in the Cohort 2a arm (randomized under Protocol Version 2.0)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)

Reporting group description:

Participants received VIT-2763 60 mg (2 x 30 mg capsules), orally, BID for 8 weeks.

Reporting group title	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)

Reporting group description:

Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, BID for 8 weeks.

Reporting group title	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)

Reporting group description:

Participants received VIT-2763 120 mg (2 x 60 mg capsules), orally, TID for 8 weeks.

Reporting group title	Cohort 4: Placebo

Reporting group description:

Participants received placebo capsules, orally, BID or TID for 8 weeks.

Reporting group title	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)

Reporting group description:

One participant received VIT-2763 30 mg, orally, BID for 8 weeks under Protocol Version 2.0. However, after the implementation of Protocol Version 3.0 and higher, this participant was excluded from the efficacy analysis and only safety data were reported (as planned).

Serious adverse events	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (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
Sickle cell anaemia with crisis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (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			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (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

Serious adverse events	Cohort 4: Placebo	Cohort 2a: VIT-2763 30 mg BID (60 mg/day)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sickle cell anaemia with crisis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: VIT-2763 60 mg BID (120 mg/Day)	Cohort 2: VIT-2763 120 mg BID (240 mg/Day)	Cohort 3: VIT-2763 120 mg TID (360 mg/Day)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	4 / 6 (66.67%)	5 / 6 (83.33%)

Vascular disorders			
Pallor			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
White blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
Sickle cell disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Migraine			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	4	1	3
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Thrombocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin depigmentation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Joint stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 4: Placebo	Cohort 2a: VIT-2763	

		30 mg BID (60 mg/day)	
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 6 (83.33%)	1 / 1 (100.00%)	
Vascular disorders Pallor subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 1 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 1 (100.00%) 1	
Cough subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 1 (100.00%) 1	
Investigations White blood cell count increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Congenital, familial and genetic disorders Sickle cell disease subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	

Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Sickle cell anaemia with crisis			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Thrombocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eye pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin depigmentation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Joint stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 1 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2021	• Dosing was changed from QD to BID, 12 hours apart. • The contraceptive advice was updated to state that abstinence should only be used as a contraceptive method if it is in line with the participants' usual and preferred lifestyle and that periodic abstinence is not an acceptable method of contraception. • Inclusion Criterion 4 was added to exclude participants with low ferritin levels. • Exclusion Criterion 11 was added to exclude participants with evidence of pulmonary hypertension. • Exclusion Criteria 13 was revised to exclude participants with QTc interval is greater than (>) 450 milliseconds (msec). • Added primary and secondary endpoints. • Added the definition of the end of study. • Added criteria for stopping IP based on ferritin level and Unexpected clinically relevant worsening of complications related to SCD. • Updated the unblinding procedure in case of emergency. • Added iron chelation therapy and RBC transfusion as prohibited therapy and concomitant treatment. • Added total iron binding capacity to the list of central laboratory assays. • Specified that signs and symptoms of SCD that have unexpectedly worsened in severity or frequency or changed in nature during the study should be recorded as AEs/SAEs. • Specified the study population to be analyzed.
09 March 2022	• Updated Sponsor contacts and Medical Monitor. • Revised study design and cohorts. • Revised expected participant duration to a maximum of 16 weeks. • Updated Nonclinical Safety Data. • Updated Summary of Completed Clinical Studies to include recent data for Studies VIT-2763-101 and VIT-2763-THAL-201. • Added Justification of Safety and Dose. • Revised criterion for withdrawal of participants from IP. • Updated treatment arms and dosing and administration guidelines. • Clarified procedures for overdose of vamifeport. • Updated risks/precautions. • Updated assessments before randomization to add total serum iron, serum ferritin, serum transferrin, calculated TSAT, hepcidin, and erythropoietin (central laboratory assessment) and clarified that full haematology panel/RBC indices (to determine baseline value) was to be done before randomization. Deleted vamifeport PK sample before randomization. • Revised study procedures for administration of first dose of IP. • Deleted 12-lead ECG assessment 3 hours post-morning dose at Visits 3, 4, and 6, and added 12-lead ECG assessment at Visit 3 at 2 hours (±30 minutes) post-morning dose. • Added total serum iron, serum ferritin, serum transferrin, calculated TSAT, hepcidin, and erythropoietin (central laboratory assessment) at Visits 3 and 5. • Added collection of additional PK samples, samples for total serum iron, serum ferritin, serum transferrin, calculated TSAT, hepcidin, and erythropoietin (central laboratory assessment), and a 2-hour post-morning dose 12-lead ECG to Visit 4. • Added 2-hour post-morning dose 12-lead ECG to Visit 5 and Visit 6 and revised the timing of sample collection for total serum iron, serum ferritin, serum transferrin, calculated TSAT, hepcidin, and erythropoietin (central laboratory assessment) to 2 hours post-morning dose. • Deleted PK sample collection at Visit 6 and added collection of samples for total serum iron, serum ferritin, serum transferrin, calculated TSAT.

16 March 2023	• Updated Co-ordinating Investigator and Sponsor contacts and Medical Expert. • Added assessment of safety and tolerance of vamifeport in patients with SCD as a secondary study objective. • Clarified the administration schedule for the vamifeport 120 mg total daily dose. • Clarified Inclusion Criterion 3 and 7. • Updated Inclusion Criterion 9. • Clarified Exclusion Criterion 1. • Updated Exclusion Criterion 5,12, 18, and 19. • Clarified BID dosing schedule. • Added exploratory PK parameters. • Clarified Morning IP dose needs to be taken at the site. • Added procedure for missed or delayed dose, allowed adaptations for assessments, operational management at the sites for Visit 4, optional blood sample for SCD genotyping, and clarify hydroxyurea administration together with contraception. • Revised the purpose of 2 blood samples at the screening visit and timing of dose administration. • Revised timing of dose administration. • Added optional blood sample for SCD genotyping. • Minor editorial and document formatting revisions were made throughout.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported