Clinical trial results:
A Phase 2a, Double-blind, Randomised, Placebo-controlled, Parallel Group, Multicentre Study on Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Preliminary Efficacy of Multiple Doses of VIT-2763 in Subjects with Non-transfusion Dependent Beta-thalassaemia.

Summary

EudraCT number	2019-002221-29
Trial protocol	GR IT
Global end of trial date	03 November 2021

Results information

Result version number	v1 (current)
This version publication date	02 November 2022
First version publication date	02 November 2022

Trial information

Trial identification

Sponsor protocol code	VIT-2763-THAL-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04364269
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vifor (International) Inc.
Sponsor organisation address	Rechenstrasse 37, St. Gallen, Switzerland, CH-9001
Public contact	VIT-2763-THAL-201 Clinical Study Team, Vifor Pharma, Inc., +41 58 852 90 74, VIT2763-THAL-201.clinicaldevelopment@viforpharma.com
Scientific contact	VIT-2763-THAL-201 Clinical Study Team, Vifor Pharma, Inc., +41 58 852 90 74, VIT2763-THAL-201.clinicaldevelopment@viforpharma.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	11 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2021
Global end of trial reached?	Yes
Global end of trial date	03 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of VIT-2763 versus placebo in adults and adolescents subjects with non-transfusion dependent thalassemia (NTDT) over a 12-week treatment period.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted. The study was conducted in compliance with the International Council for Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP). Prior to the initiation of the study, the protocol, the subject information sheet, and the informed consent form (ICF) were reviewed and approved by Independent Ethics Committees (IECs) or Institutional Review Boards (IRBs), Ethics Committee (EC) operating in accordance with current regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 June 2020
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	Lebanon: 3
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Thailand: 9
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	25
EEA total number of subjects	10

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: -

Pre-assignment

Screening details:

From a total of 35 screened participants, 25 were randomized in the study. A total of 10 participants were not randomised, among which 2 participants withdrew their consent, and 8 participants did not meet the inclusion/ exclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	VIT-2763 QD

Arm description:

Participants who received VIT-2763 once a day (QD).

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

Dosage and administration details:

VIT-2763 was administered once a day (QD), in a total daily dose of 60 mg or 120 mg, depending on participant's body weight, during 12 weeks. Participants received VIT-2763 QD at a dose of 60 mg if their body weight was between 40 kg to 59 kg or at a dose of 120 mg if their body weight was between 60 kg and 100 kg. The study medication (VIT-2763 and/or matching placebo) was administered to all participants twice a day to maintain the blind. VIT-2763 capsules were administered approximately 1 hour after meals at the same clock time (between 08:00 and 10:00 for the morning dose, and between 20:00 and 22:00 for the evening dose, respectively). Food intake, except for water ad libitum, was to be avoided for at least 1 hour prior to and 1 hour after the morning and evening dose administration.

Arm title	VIT-2763 BID

Arm description:

Participants who received VIT-2763 twice daily (BID).

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

Dosage and administration details:

VIT-2763 was administered twice a day (BID) in a total daily dose of 60 mg or 120 mg, depending on participant's body weight, during 12 weeks. Participants received VIT-2763 BID at a dose of 60 mg if their body weight was between 40 kg to 59 kg or at a dose of 120 mg if their body weight was between 60 kg and 100 kg. VIT-2763 capsules were administered approximately 1 hour after meals at the same clock time (between 08:00 and 10:00 for the morning dose, and between 20:00 and 22:00 for the evening dose, respectively). Food intake, except for water ad libitum, was to be avoided for at least 1 hour prior to and 1 hour after the morning and evening dose administration.

Arm title	Placebo

Arm description:

Participants who received placebo twice daily.

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

Dosage and administration details:

Placebo was administered twice a day (BID) in a total daily dose of 60 mg or 120 mg, depending on participant's body weight, during 12 weeks. Participants received placebo at a dose of 60 mg if their body weight was between 40 kg to 59 kg or at a dose of 120 mg if their body weight was between 60 kg and 100 kg. Placebo capsules were administered approximately 1 hour after meals at the same clock time (between 08:00 and 10:00 for the morning dose, and between 20:00 and 22:00 for the evening dose, respectively). Food intake, except for water ad libitum, was to be avoided for at least 1 hour prior to and 1 hour after the morning and evening dose administration.

Number of subjects in period 1	VIT-2763 QD	VIT-2763 BID	Placebo
Started	9	12	4
Completed	8	11	4
Not completed	1	1	0
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	VIT-2763 QD
Reporting group description:	
Participants who received VIT-2763 once a day (QD).	
Reporting group title	VIT-2763 BID
Reporting group description:	
Participants who received VIT-2763 twice daily (BID).	
Reporting group title	Placebo
Reporting group description:	
Participants who received placebo twice daily.	

Reporting group values	VIT-2763 QD	VIT-2763 BID	Placebo
Number of subjects	9	12	4
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	9	12	4
>=65 years	0	0	0
Gender categorical Units: Subjects			
Female	6	2	1
Male	3	10	3

Reporting group values	Total		
Number of subjects	25		
Age categorical Units: Subjects			
<=18 years	0		
Between 18 and 65 years	25		
>=65 years	0		
Gender categorical Units: Subjects			
Female	9		
Male	16		

End points

End points reporting groups

Reporting group title	VIT-2763 QD
Reporting group description:	
Participants who received VIT-2763 once a day (QD).	
Reporting group title	VIT-2763 BID
Reporting group description:	
Participants who received VIT-2763 twice daily (BID).	
Reporting group title	Placebo
Reporting group description:	
Participants who received placebo twice daily.	

Primary: Number of Participants With TEAEs

End point title	Number of Participants With TEAEs[1]

End point description:

Please note that in this section we are presenting just the overview of the adverse events experienced by the trial participants, in particular, the number of participants with at least one TEAE. Please refer to the detailed tables included on the Adverse Event Module for specifics.

TEAEs = Treatment-Emergent Adverse Events

End point type	Primary

End point timeframe:

From baseline to Week 16.

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 analysis is descriptive. No inferential statistics were performed to compare treatment groups.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: Number				
Number of Participants With TEAEs	6	7	3	

Statistical analyses

No statistical analyses for this end point

Primary: Changes in the Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)

End point title	Changes in the Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)[2]

End point description:

Summary of the values by visit from baseline and changes from baseline by post-baseline visit.

End point type	Primary

End point timeframe:

From baseline to Week 12.

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: The analysis is descriptive. No inferential statistics were performed to compare treatment groups.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP Baseline	114.2 (± 11.62)	114.7 (± 13.88)	114.8 (± 12.97)	
SBP Week 1	115.0 (± 8.35)	116.7 (± 10.65)	104.0 (± 8.98)	
SBP Change from Baseline to Week 1	0.8 (± 8.94)	2.0 (± 9.72)	-10.8 (± 10.90)	
SBP Week 2	113.9 (± 9.41)	118.3 (± 14.85)	114.8 (± 15.06)	
SBP Change from Baseline to Week 2	-0.3 (± 6.60)	3.6 (± 8.78)	0.0 (± 2.83)	
SBP Week 4	112.0 (± 11.20)	113.9 (± 12.41)	104.8 (± 6.85)	
SBP Change from Baseline to Week 4	-2.2 (± 8.77)	-0.8 (± 8.51)	-10.0 (± 14.72)	
SBP Week 8	114.9 (± 7.41)	113.8 (± 10.54)	109.8 (± 12.61)	
SBP Change from Baseline to Week 8	0.7 (± 11.11)	0.9 (± 9.63)	-5.0 (± 1.63)	
SBP Week 12	113.4 (± 11.02)	112.8 (± 11.31)	107.5 (± 10.08)	
SBP Change from Baseline to Week 12	-0.8 (± 13.02)	-0.1 (± 10.85)	-7.3 (± 3.40)	
DBP Baseline	65.94 (± 10.088)	65.00 (± 10.189)	66.50 (± 7.853)	
DBP Week 1	66.44 (± 6.710)	69.33 (± 9.921)	61.75 (± 4.856)	
DBP Change from Baseline to Week 1	0.50 (± 4.886)	4.33 (± 6.344)	-4.75 (± 6.185)	
DBP Week 2	65.89 (± 9.545)	68.83 (± 11.535)	64.00 (± 6.055)	
DBP Change from Baseline to Week 2	-0.06 (± 5.353)	3.83 (± 8.726)	-2.50 (± 3.000)	
DBP Week 4	65.22 (± 11.043)	62.33 (± 9.069)	62.75 (± 3.775)	
DBP Change from Baseline to Week 4	-0.72 (± 9.398)	-2.67 (± 9.921)	-3.75 (± 5.058)	
DBP Week 8	63.44 (± 6.579)	67.18 (± 9.174)	66.75 (± 7.500)	
DBP Change from Baseline to Week 8	-2.50 (± 8.216)	3.27 (± 8.439)	0.25 (± 7.848)	
DBP Week 12	63.67 (± 7.697)	67.64 (± 9.657)	62.50 (± 3.317)	
DBP Change from Baseline to Week 12	-2.28 (± 10.140)	3.73 (± 6.310)	-4.00 (± 6.880)	

Statistical analyses

No statistical analyses for this end point

Primary: Changes in the Heart Rate

End point title	Changes in the Heart Rate[3]

End point description:

Summary of the values by visit from baseline and changes from baseline by post-baseline visit.

End point type	Primary

End point timeframe:

From baseline to Week 12.

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 analysis is descriptive. No inferential statistics were performed to compare treatment groups.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: Pulse Rate (bpm)				
arithmetic mean (standard deviation)				
Baseline	82.00 (± 12.135)	77.71 (± 10.208)	73.75 (± 5.560)	
Week 1	82.33 (± 11.694)	80.33 (± 9.875)	70.75 (± 6.449)	
Change from Baseline to Week 1	0.33 (± 6.042)	2.63 (± 5.859)	-3.00 (± 5.715)	
Week 2	83.56 (± 12.856)	75.83 (± 9.953)	75.00 (± 8.756)	
Change from Baseline to Week 2	1.56 (± 10.442)	-1.88 (± 8.263)	1.25 (± 3.775)	
Week 4	82.33 (± 14.414)	77.92 (± 9.830)	73.25 (± 3.775)	
Change from Baseline to Week 4	0.33 (± 8.818)	0.21 (± 5.541)	-0.50 (± 1.915)	
Week 8	83.22 (± 11.322)	80.27 (± 10.992)	72.50 (± 5.196)	
Change from Baseline to Week 8	1.22 (± 6.648)	2.68 (± 9.040)	-1.25 (± 7.411)	

Statistical analyses

No statistical analyses for this end point

Primary: Changes in 12-lead Electrocardiogram (ECG) Parameters

End point title	Changes in 12-lead Electrocardiogram (ECG) Parameters[4]

End point description:

Values by visit from baseline and changes from baseline by post-baseline visit for PR interval, QRS duration, QT interval and QTcF interval.

PR interval represents the time from the onset of the P wave to the start of the QRS complex. QRS duration represents the time required for a stimulus to spread through the ventricles (ventricular depolarization). QT interval represents the time from the start of the Q wave to the end of the T wave.

RR interval represents the time from the onset of one R wave to the onset of the next one, one complete cardiac cycle. QT corrected for heart rate (QTc) interval reflects ventricular repolarization. BAS = Baseline.

End point type	Primary

End point timeframe:

From baseline to Week 12.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis is descriptive. No inferential statistics were performed to compare treatment groups.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: milliseconds (ms)				
arithmetic mean (standard deviation)				
PR interval - BAS	158.3 (± 25.14)	147.6 (± 20.05)	175.8 (± 38.92)	
PR interval - BAS 2h post-dose	161.2 (± 21.28)	155.1 (± 17.98)	175.0 (± 14.07)	
PR interval - Change from BAS to BAS 2h post-dose	2.9 (± 25.78)	6.3 (± 16.45)	-0.8 (± 38.59)	
PR interval - Week 1	159.2 (± 22.90)	153.0 (± 14.12)	189.5 (± 18.72)	
PR interval - Change from BAS to Week 1	0.9 (± 16.59)	4.7 (± 12.71)	13.8 (± 25.67)	
PR interval - Week 2	167.6 (± 26.49)	153.0 (± 17.87)	185.5 (± 4.43)	
PR interval - Change from BAS to Week 2	9.2 (± 27.64)	5.5 (± 13.56)	9.8 (± 37.56)	
PR interval - Week 4	154.0 (± 26.49)	154.2 (± 21.19)	185.0 (± 7.39)	
PR interval - Change from BAS to Week 4	-4.3 (± 18.85)	8.1 (± 15.48)	9.3 (± 33.42)	
PR interval - Week 8	161.2 (± 19.34)	153.5 (± 20.61)	185.8 (± 10.14)	
PR interval - Change from BAS to Week 8	2.9 (± 17.05)	7.1 (± 12.66)	10.0 (± 32.86)	
PR interval - Week 12	160.6 (± 19.55)	156.6 (± 14.47)	182.8 (± 11.98)	
PR interval - Change from BAS to Week 12	2.2 (± 19.50)	11.5 (± 14.25)	7.0 (± 36.09)	
QRS duration - BAS	94.0 (± 18.73)	88.8 (± 19.17)	119.3 (± 50.12)	
QRS duration - BAS 2h post-dose	94.3 (± 20.20)	95.8 (± 10.96)	85.0 (± 11.60)	
QRS duration - Change from BAS to BAS 2h post-dose	0.3 (± 4.82)	7.0 (± 14.39)	-34.3 (± 55.27)	
QRS duration - Week 1	98.4 (± 23.16)	96.1 (± 11.27)	98.0 (± 16.57)	
QRS duration - Change from BAS to Week 1	4.4 (± 14.75)	7.3 (± 13.45)	-21.3 (± 65.76)	
QRS duration - Week 2	94.0 (± 29.01)	96.3 (± 14.13)	91.3 (± 12.09)	
QRS duration - Change from BAS to Week 2	0.0 (± 23.04)	7.6 (± 17.96)	-28.0 (± 61.36)	
QRS duration - Week 4	92.3 (± 23.32)	92.6 (± 15.11)	94.3 (± 8.10)	
QRS duration - Change from BAS to Week 4	-1.7 (± 11.16)	6.0 (± 16.76)	-25.0 (± 54.02)	
QRS duration - Week 8	91.0 (± 24.72)	94.9 (± 18.27)	93.3 (± 10.81)	

QRS duration - Change from BAS to Week 8	-3.0 (± 15.99)	7.4 (± 28.52)	-26.0 (± 60.02)	
QRS duration - Week 12	94.3 (± 27.31)	84.8 (± 18.66)	91.8 (± 10.59)	
QRS duration - Change from BAS to Week 12	0.3 (± 20.64)	-2.7 (± 23.70)	-27.5 (± 60.69)	
QT interval - BAS	371.7 (± 76.41)	374.2 (± 21.78)	420.8 (± 48.75)	
QT interval - BAS 2h post-dose	385.7 (± 50.89)	376.8 (± 22.25)	379.5 (± 30.17)	
QT interval - Change from BAS to BAS 2h post-dose	14.0 (± 61.00)	2.6 (± 21.49)	-41.3 (± 68.30)	
QT interval - Week 1	394.1 (± 47.36)	374.8 (± 33.12)	381.5 (± 32.18)	
QT interval - Change from BAS to Week 1	22.4 (± 57.20)	0.7 (± 28.96)	-39.3 (± 71.63)	
QT interval - Week 2	384.0 (± 55.52)	367.0 (± 24.68)	378.3 (± 27.89)	
QT interval - Change from BAS to Week 2	12.3 (± 76.14)	-7.2 (± 27.61)	-42.5 (± 61.87)	
QT interval - Week 4	370.1 (± 67.13)	373.6 (± 21.22)	378.0 (± 36.51)	
QT interval - Change from BAS to Week 4	-1.6 (± 23.07)	0.9 (± 24.94)	-42.8 (± 61.50)	
QT interval - Week 8	389.7 (± 39.20)	379.4 (± 25.08)	381.8 (± 37.99)	
QT interval - Change from BAS to Week 8	18.0 (± 69.60)	4.6 (± 22.59)	-39.0 (± 64.59)	
QT interval - Week 12	380.9 (± 59.97)	364.2 (± 36.22)	388.3 (± 42.85)	
QT interval - Change from BAS to Week 12	9.2 (± 33.53)	-10.5 (± 33.69)	-32.5 (± 72.06)	
RR interval - BAS	789.4 (± 128.89)	801.4 (± 95.56)	877.5 (± 114.65)	
RR interval - BAS 2h post-dose	781.2 (± 155.21)	805.5 (± 119.36)	812.5 (± 124.38)	
RR interval - Change from BAS to BAS 2h post-dose	-8.2 (± 87.78)	4.1 (± 112.91)	-65.0 (± 196.09)	
RR interval - Week 1	793.2 (± 105.35)	864.9 (± 149.33)	826.5 (± 96.57)	
RR interval - Change from BAS to Week 1	3.8 (± 82.82)	63.5 (± 137.59)	-51.0 (± 98.80)	
RR interval - Week 2	757.3 (± 120.25)	830.1 (± 138.34)	833.8 (± 16.01)	
RR interval - Change from BAS to Week 2	-32.1 (± 146.70)	28.7 (± 117.34)	-43.8 (± 103.92)	
RR interval - Week 4	783.7 (± 110.55)	829.8 (± 154.72)	825.8 (± 96.08)	
RR interval - Change from BAS to Week 4	-5.8 (± 62.11)	34.1 (± 137.64)	-51.8 (± 111.05)	
RR interval - Week 8	765.0 (± 91.52)	810.1 (± 138.16)	844.8 (± 135.47)	
RR interval - Change from BAS to Week 8	-24.4 (± 116.42)	17.2 (± 108.39)	-32.8 (± 152.45)	
RR interval - Week 12	780.7 (± 140.88)	812.9 (± 93.89)	878.3 (± 133.70)	
RR interval - Change from BAS to Week 12	-8.8 (± 115.95)	20.0 (± 73.46)	0.8 (± 172.81)	
QTcF interval - BAS	403.3 (± 80.48)	400.5 (± 22.76)	416.8 (± 17.46)	
QTcF interval - BAS 2h post-dose	419.3 (± 36.58)	410.1 (± 25.34)	407.3 (± 13.05)	

QTcF interval - Change from BAS to BAS 2h post-dos	16.0 (± 66.51)	9.6 (± 22.60)	-9.5 (± 6.76)	
QTcF interval - Week 1	425.7 (± 37.25)	397.3 (± 30.44)	406.8 (± 26.02)	
QTcF interval - Change from BAS to Week 1	22.3 (± 65.53)	-3.3 (± 24.92)	-10.0 (± 20.38)	
QTcF interval - Week 2	420.8 (± 42.28)	393.3 (± 28.90)	402.0 (± 30.30)	
QTcF interval - Change from BAS to Week 2	17.4 (± 77.84)	-7.2 (± 27.52)	-14.8 (± 14.52)	
QTcF interval - Week 4	401.3 (± 64.21)	401.8 (± 27.41)	402.8 (± 23.63)	
QTcF interval - Change from BAS to Week 4	-2.0 (± 24.74)	2.1 (± 24.41)	-14.0 (± 7.07)	
QTcF interval - Week 8	426.0 (± 30.12)	399.6 (± 27.17)	404.3 (± 19.86)	
QTcF interval - Change from BAS to Week 8	22.7 (± 80.36)	0.3 (± 26.86)	-12.5 (± 4.51)	
QTcF interval - Week 12	414.1 (± 53.40)	391.4 (± 42.91)	405.3 (± 25.71)	
QTcF interval - Change from BAS to Week 12	10.8 (± 37.94)	-8.0 (± 37.96)	-11.5 (± 10.63)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Serum Iron

End point title	Change From Baseline in Total Serum Iron

End point description:

Assessment of total serum Iron from baseline over a 12-week period (absolute and change from baseline). For the serum iron parameter, the 'Baseline' was collected during the screening period within the biochemistry sample.

End point type	Secondary

End point timeframe:

From baseline to Week 12.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: Micromoles per Litre (umol/L)				
arithmetic mean (standard deviation)				
Baseline	23.81 (± 13.438)	28.42 (± 9.796)	30.88 (± 13.329)	
Week 1	12.54 (± 9.159)	11.38 (± 7.693)	28.20 (± 17.919)	
Change from Baselines to Week 1	-11.27 (± 7.158)	-17.03 (± 9.611)	-2.68 (± 12.365)	
Week 2	11.71 (± 8.622)	12.99 (± 8.978)	32.48 (± 15.541)	
Change from Baseline to Week 2	-9.74 (± 4.707)	-15.43 (± 12.784)	1.60 (± 3.996)	

Week 4	13.90 (± 12.222)	12.85 (± 7.583)	31.08 (± 13.721)	
Change from Baseline to Week 4	-9.33 (± 4.659)	-14.03 (± 8.432)	0.20 (± 2.902)	
Week 8	11.35 (± 7.822)	11.55 (± 9.651)	26.70 (± 12.040)	
Change from Baseline to Week 8	-11.88 (± 9.627)	-17.05 (± 11.936)	-0.37 (± 3.550)	
Week 12	13.72 (± 11.031)	11.62 (± 6.442)	27.10 (± 12.856)	
Change from Baseline to Week 12	-10.54 (± 6.782)	-16.22 (± 10.892)	0.03 (± 2.701)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Ferritin

End point title	Change From Baseline in Serum Ferritin

End point description:

Assessment of serum ferritin from baseline over a 12-week period (absolute and change from baseline). For the serum ferritin parameter, the 'Baseline' was collected during the screening period within the biochemistry sample.

End point type	Secondary

End point timeframe:

From baseline to Week 12.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: Micrograms per Litre (ug/L)				
arithmetic mean (standard deviation)				
Baseline	403.14 (± 226.315)	1133.23 (± 2119.115)	440.03 (± 321.453)	
Week 1	416.76 (± 220.567)	471.53 (± 209.800)	445.80 (± 228.244)	
Change from Baseline to Week 1	-10.14 (± 31.509)	40.89 (± 164.466)	5.77 (± 93.946)	
Week 2	441.34 (± 269.599)	500.79 (± 230.076)	411.35 (± 207.477)	
Change from Baseline to Week 2	3.29 (± 60.579)	23.80 (± 149.147)	-49.80 (± 76.867)	
Week 4	476.60 (± 282.457)	585.71 (± 311.224)	389.83 (± 240.553)	
Change from Baseline to Week 4	1.05 (± 61.638)	89.98 (± 249.397)	-50.20 (± 80.958)	
Week 8	463.67 (± 206.646)	508.56 (± 211.366)	340.23 (± 165.356)	
Change from Baseline to Week 8	-11.88 (± 43.063)	52.84 (± 157.952)	-9.45 (± 20.577)	
Week 12	465.72 (± 227.378)	927.42 (± 1478.471)	261.70 (± 53.033)	

Change from Baseline to Week 12	-15.84 (± 66.208)	-139.23 (± 626.380)	7.25 (± 57.205)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Transferrin

End point title	Change From Baseline in Serum Transferrin

End point description:

Assessment of serum transferrin from baseline over a 12-week period (absolute and change from baseline). For the serum transferrin parameter, the "Baseline 2h post-dose" was defined as the value at Visit 3 2h post-dose.

End point type	Secondary

End point timeframe:

From baseline to Week 12.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: Grammes per Litre (g/L)				
arithmetic mean (standard deviation)				
Baseline 2h post-dose	1.601 (± 0.4377)	1.673 (± 0.3177)	1.655 (± 0.3003)	
Week 1	1.610 (± 0.4557)	1.822 (± 0.3903)	1.683 (± 0.2210)	
Change from Baseline to Week 1	0.009 (± 0.1184)	0.149 (± 0.1334)	0.028 (± 0.2419)	
Week 2	1.601 (± 0.5043)	1.759 (± 0.3569)	1.655 (± 0.2408)	
Change from Baseline to Week 2	-0.014 (± 0.1516)	0.087 (± 0.1429)	0.000 (± 0.1846)	
Week 4	1.708 (± 0.2672)	1.705 (± 0.3496)	1.745 (± 0.3756)	
Change from Baseline to Week 4	0.053 (± 0.2014)	0.054 (± 0.1535)	0.090 (± 0.2740)	
Week 8	1.640 (± 0.2745)	1.725 (± 0.3194)	1.553 (± 0.2836)	
Change from Baseline to Week 8	-0.015 (± 0.0675)	0.093 (± 0.1618)	-0.120 (± 0.0854)	
Week 12	1.706 (± 0.1954)	1.656 (± 0.2974)	1.610 (± 0.4784)	
Change from Baseline to Week 12	-0.040 (± 0.1116)	0.100 (± 0.1044)	-0.063 (± 0.1266)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Calculated Transferrin Saturation (TSAT)

End point title	Change From Baseline in Calculated Transferrin Saturation (TSAT)

End point description:

Assessment of TSAT from baseline over a 12-week period (absolute and change from baseline). For the calculated transferrin saturation parameter, the 'Baseline' was collected during the screening period within the biochemistry sample. Transferrin Saturation (TSAT) was calculated as Total Iron /Total Iron Binding Capacity (TIBC) X 100.

End point type	Secondary

End point timeframe:

From baseline to Week 12.

End point values	VIT-2763 QD	VIT-2763 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	12	4	
Units: Percentage (%)				
arithmetic mean (standard deviation)				
Baseline	69.3 (± 31.16)	79.0 (± 24.05)	83.3 (± 33.50)	
Week 1	36.8 (± 24.44)	32.2 (± 21.44)	56.5 (± 30.56)	
Change from Baselone to Week 1	-32.6 (± 19.55)	-46.8 (± 22.55)	-26.8 (± 28.77)	
Week 2	36.0 (± 22.81)	35.8 (± 24.13)	71.5 (± 33.91)	
Change from Baseline to Week 2	-29.5 (± 14.57)	-43.2 (± 33.23)	-11.8 (± 23.50)	
Week 4	41.0 (± 32.27)	38.4 (± 24.85)	82.5 (± 35.00)	
Change from Baseline to Week 4	-24.0 (± 18.21)	-38.7 (± 27.57)	-0.8 (± 1.50)	
Week 8	32.3 (± 17.48)	33.5 (± 27.08)	77.3 (± 39.26)	
Change from Baseline to Week 8	-32.7 (± 25.80)	-47.9 (± 29.70)	-0.3 (± 0.58)	
Week 12	36.0 (± 25.93)	34.8 (± 17.76)	76.3 (± 40.99)	
Change from Baseline to Week 12	-27.6 (± 20.37)	-46.8 (± 23.61)	-1.3 (± 2.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics Parameters - VIT-2763 Plasma Concentration Over Time

End point title	Pharmacokinetics Parameters - VIT-2763 Plasma Concentration Over Time[5]

End point description:

Sparse sampling for determination of VIT-2763 plasma concentration following multiple dosing was obtained from predose trough to 3 hours or 4 hours post-dose at selected study visits. Pharmacokinetics parameters (Cmax, clearance, distribution volume, area under the curve (AUC) were not calculated for the study.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 8 and Week 12.

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: There are no results of PK parameters applicable for the Placebo arm.

End point values	VIT-2763 QD	VIT-2763 BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Visit 3 1 hour post-dose	796.5 (± 508.2)	609.6 (± 455.2)		
Visit 3 4 hours post-dose	222.3 (± 73.1)	411.0 (± 269.5)		
Visit 6 pre-dose	17.2 (± 10.2)	114.4 (± 78.2)		
Visit 6 1 hour post-dose	986.2 (± 796.7)	483.5 (± 247.3)		
Visit 6 3 hours post-dose	578.2 (± 494.5)	544.3 (± 337.5)		
Visit 7 pre-dose	15.5 (± 6.6)	111.0 (± 61.9)		
Visit 7 1 hour post-dose	751.7 (± 682.3)	692.2 (± 470.2)		
Visit 7 4 hours post-dose	295.5 (± 209.5)	384.3 (± 200.9)		
Visit 8 pre-dose	361.5 (± 579.2)	136.0 (± 76.8)		
Visit 8 1 hour post-dose	894.1 (± 670.3)	650.6 (± 474.5)		
Visit 8 3 hours post-dose	684.0 (± 405.5)	569.9 (± 343.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall study	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0
Reporting groups	
Reporting group title	VIT-2763 QD
Reporting group description:	
Participants who received VIT-2763 once a day (QD).	
Reporting group title	VIT-2763 BID
Reporting group description:	
Participants who received VIT-2763 twice daily (BID).	
Reporting group title	Placebo
Reporting group description:	
Participants who received placebo twice daily.	

Serious adverse events	VIT-2763 QD	VIT-2763 BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	VIT-2763 QD	VIT-2763 BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 9 (66.67%)	7 / 12 (58.33%)	3 / 4 (75.00%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 9 (22.22%)	2 / 12 (16.67%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pyrexia			

subjects affected / exposed	0 / 9 (0.00%)	2 / 12 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory symptom			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	1 / 9 (11.11%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Presyncope			

subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Haemolysis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Eye disorders			
Photopsia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vitreous floaters			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 12 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Faeces discoloured			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Jaundice			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2019	Version 2.0
10 December 2020	Version 3.0
12 April 2021	Version 4.0 (final)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported