



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 occurrences (all) | 1 / 6 (16.67%) 1 | 2 / 6 (33.33%) 2 | 0 / 6 (0.00%) 0 |
| Migraine subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood and lymphatic system disorders Sickle cell anaemia with crisis subjects affected / exposed occurrences (all) | 3 / 6 (50.00%) 4 | 1 / 6 (16.67%) 1 | 2 / 6 (33.33%) 3 |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Thrombocytosis subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Eye pruritus subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Skin depigmentation subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 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 | 0 / 6 (0.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 1 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 1 (100.00%) | |
| occurrences (all) | 0 | 1 | |
| Cough | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 1 (100.00%) | |
| occurrences (all) | 1 | 1 | |
| Investigations | | | |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Congenital, familial and genetic disorders | | | |
| Sickle cell disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 0 | 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 occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 1 (0.00%) 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 | 1 / 6 (16.67%) | 0 / 1 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 03 March 2021 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• 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 vamiporto.• 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 vamiporto 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 | <ul style="list-style-type: none"> • 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