



Clinical trial results:

A Phase 2 Open-Label Study to Evaluate Etavopivat for the Treatment of Anemia in Patients with Myelodysplastic Syndromes (MDS)

Summary

EudraCT number	2022-001253-23
Trial protocol	FR
Global end of trial date	15 July 2024

Results information

Result version number	v1 (current)
This version publication date	31 July 2025
First version publication date	31 July 2025

Trial information

Trial identification

Sponsor protocol code	4202-ONC-203
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05568225
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Novo Nordisk A/S, Clinical Reporting Office (2834), clinicaltrials@novonordisk.com
Scientific contact	Novo Nordisk A/S, Clinical Reporting Office (2834), clinicaltrials@novonordisk.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	06 September 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 July 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess hematologic improvement based on an erythroid response (HI E) greater than or equal to ($\geq$) 8 weeks duration in subjects with MDS within 24 weeks of etavopivat treatment

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (Oct 2013) and International Council for Harmonisation (ICH) Good Clinical Practice, including archiving of essential documents (May 1996) and European Standard (EN) International Standard (ISO) 14155 Part 1 and 2 and Food and Drug Administration (FDA) 21 Code of Federal Regulations (CFR) 312.120.

Background therapy:

Etavopivat is a selective, orally bioavailable small-molecule activator of the red blood cell pyruvate kinase (PKR) enzyme. By activating PKR, etavopivat aims to increase the production of adenosine triphosphate (ATP) in red blood cells, which is hypothesized to enhance haemoglobin levels and improve erythroid response. This mechanism is particularly relevant for subjects with myelodysplastic syndromes (MDS), where anaemia and reduced red blood cell production are significant concerns.

Subjects in the study were classified into groups based on their risk levels: very low risk, low risk, or intermediate risk MDS. This categorization was important for assessing the therapy's effectiveness and safety in different subject subpopulations, ensuring tailored evaluation of responses to etavopivat and its impact on anaemia management.

Evidence for comparator:

Not applicable

Actual start date of recruitment	15 November 2022
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	United States: 5
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	France: 2
Worldwide total number of subjects	17
EEA total number of subjects	6

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)	3
From 65 to 84 years	12
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 10 sites in 4 countries.

Pre-assignment

Screening details:

Of the 45 subjects targeted, only 24 were screened, and 17 were enrolled into three groups: Non-transfusion dependent (NTD) N=3, Low transfusion burden (LTB) N=5, and High transfusion burden (HTB) N=9. Each subject received 400 mg of etavopivat daily.

Period 1

Period 1 title	Primary treatment period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Non-transfusion dependent

Arm description:

Non transfusion dependent subjects who had received less than equal to ($\leq$) 2 red blood cell (RBC) transfusions for anaemia within the prior 16 weeks, orally received 400 milligram (mg) of etavopivat once daily for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Etavopivat
Investigational medicinal product code	FT-4202
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Etavopivat was administrated to subjects as two oral tablets of 200 mg each once daily (daily dosage-400 mg).

Arm title	Low transfusion burden
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Arm description:

Low transfusion burden subjects who had received 3 to 7 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Etavopivat
Investigational medicinal product code	FT-4202
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Etavopivat was administrated to subjects as two oral tablets of 200 mg each once daily (daily dosage-400 mg).

Arm title	High transfusion burden
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Arm description:

High transfusion burden subjects who had received $\geq$ 8 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Arm type	Experimental
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Investigational medicinal product name	Etavopivat
Investigational medicinal product code	FT-4202
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Etavopivat was administrated to subjects as two oral tablets of 200 mg each once daily (daily dosage-400 mg).

Number of subjects in period 1	Non-transfusion dependent	Low transfusion burden	High transfusion burden
Started	3	5	9
Efficacy evaluable set (EES)	1	2	4
Safety Population	3	5	9
Full analysis set (FAS)	3	5	9
Pharmacokinetic Population	3	5	9
Completed	1	2	4
Not completed	2	3	5
Physician decision	-	1	-
Disease progression	-	1	-
Adverse event, non-fatal	1	-	-
Termination of the study by the Sponsor	-	-	1
Withdrawal of consent	1	-	4
Lack of efficacy	-	1	-

Period 2

Period 2 title	Extension treatment period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Non-transfusion dependent

Arm description:

Non transfusion dependent subjects who had received ≤ 2 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Arm type	Experimental
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Investigational medicinal product name	Etavopivat
Investigational medicinal product code	FT-4202
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Etavopivat was administrated to subjects as two oral tablets of 200 mg each once daily (daily dosage-400 mg).

Arm title	Low transfusion burden
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Arm description:

Low transfusion burden subjects who had received 3 to 7 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Etavopivat
Investigational medicinal product code	FT-4202
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Etavopivat was administrated to subjects as two oral tablets of 200 mg each once daily (daily dosage-400 mg).

Arm title	High transfusion burden
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Arm description:

High transfusion burden subjects who had received ≥ 8 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Etavopivat
Investigational medicinal product code	FT-4202
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Etavopivat was administrated to subjects as two oral tablets of 200 mg each once daily (daily dosage-400 mg).

Number of subjects in period 2	Non-transfusion dependent	Low transfusion burden	High transfusion burden
Started	1	2	4
Completed	1	2	1
Not completed	0	0	3
Termination of the study by the Sponsor	-	-	1
Lack of efficacy	-	-	1
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Non-transfusion dependent
Reporting group description: Non transfusion dependent subjects who had received less than equal to ($\leq$) 2 red blood cell (RBC) transfusions for anaemia within the prior 16 weeks, orally received 400 milligram (mg) of etavopivat once daily for up to 48 weeks.	
Reporting group title	Low transfusion burden
Reporting group description: Low transfusion burden subjects who had received 3 to 7 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	
Reporting group title	High transfusion burden
Reporting group description: High transfusion burden subjects who had received ≥ 8 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	

Reporting group values	Non-transfusion dependent	Low transfusion burden	High transfusion burden
Number of subjects	3	5	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	3
From 65-84 years	3	4	5
85 years and over	0	1	1
Age Continuous Units: Years			
arithmetic mean	77.3	80.2	71.2
standard deviation	± 5.69	± 3.49	± 8.11
Sex: Female, Male Units: Subjects			
Female	0	1	3
Male	3	4	6

Reporting group values	Total		
Number of subjects	17		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	3		
From 65-84 years	12		
85 years and over	2		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	4		
Male	13		

End points

End points reporting groups

Reporting group title	Non-transfusion dependent
Reporting group description: Non transfusion dependent subjects who had received less than equal to ($\leq$) 2 red blood cell (RBC) transfusions for anaemia within the prior 16 weeks, orally received 400 milligram (mg) of etavopivat once daily for up to 48 weeks.	
Reporting group title	Low transfusion burden
Reporting group description: Low transfusion burden subjects who had received 3 to 7 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	
Reporting group title	High transfusion burden
Reporting group description: High transfusion burden subjects who had received ≥ 8 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	
Reporting group title	Non-transfusion dependent
Reporting group description: Non transfusion dependent subjects who had received ≤ 2 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	
Reporting group title	Low transfusion burden
Reporting group description: Low transfusion burden subjects who had received 3 to 7 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	
Reporting group title	High transfusion burden
Reporting group description: High transfusion burden subjects who had received ≥ 8 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.	

Primary: Proportion of subjects with Hematologic Improvement– Erythroid (HI-E) response for ≥ 8 weeks within 24 weeks of etavopivat treatment

End point title	Proportion of subjects with Hematologic Improvement– Erythroid (HI-E) response for ≥ 8 weeks within 24 weeks of etavopivat treatment ^[1]
End point description: This endpoint reported on the combined incidence of NTD, LTB and HTB in terms of (HI-E) response for ≥ 8 weeks duration in subjects with myelodysplastic syndromes (MDS) within 24 weeks. The subjects were allocated to the following arms which were defined as: 1) NTD: ≥ 1.5 grams per deciliter (g/dL) increase in haemoglobin (Hb) from baseline maintained ≥ 8 consecutive weeks and no transfusion of RBC units for anemia over a continuous 8-week treatment period; 2) LTB: absence of any transfusion for ≥ 8 consecutive weeks; and 3) HTB: reduction by ≥ 50 percent (%) of RBC units for ≥ 8 consecutive weeks. EES: All subjects in the FAS who had completed the week 24 response visit and who had a baseline record of the primary endpoint.	
End point type	Primary
End point timeframe: From Baseline to Week 24	
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: Statistical analyses is not required for this endpoint.	

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	2	4	
Units: Proportion of subjects				
number (not applicable)	0	50	25	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with Hematologic Improvement–Erythroid (HI-E) response for ≥ 8 weeks within 16 and 48 weeks of etavopivat

End point title	Proportion of subjects with Hematologic Improvement–Erythroid (HI-E) response for ≥ 8 weeks within 16 and 48 weeks of etavopivat
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End point description:

This endpoint focused on the combined incidence of NTD, LTB and HTB subjects, evaluating HI-E lasting ≥ 8 weeks in individuals with MDS within 16 weeks and 48 weeks. Subject's response were defined as follows: 1) NTD: an increase of ≥ 1.5 g/dL in Hb maintained for ≥ 8 consecutive weeks without any RBC transfusions for anemia; 2) LTB: no transfusions over ≥ 8 consecutive weeks; and 3) HTB: a reduction of $\geq 50\%$ in RBC units for ≥ 8 consecutive weeks. FAS: All subjects who signed the informed consent and received at least 1 dose of etavopivat. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.

End point type	Secondary
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End point timeframe:

48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	
Units: Proportion of Subjects				
number (not applicable)				

Notes:

[2] - Data for this endpoint was not analysed due to early termination of study.

[3] - Data for this endpoint was not analysed due to early termination of study.

[4] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with Hematologic Improvement– Erythroid (HI-E) response for ≥ 16 weeks within 24 and 48 weeks of etavopivat

End point title	Proportion of subjects with Hematologic Improvement–Erythroid (HI-E) response for ≥ 16 weeks within 24 and 48 weeks of etavopivat
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End point description:

This endpoint focused on the combined incidence of NDT, LTB and HTB subjects, evaluating HI-E response lasting ≥ 16 weeks in individuals with MDS within 24 weeks and 48 weeks. Subject's response were defined as follows: 1) NTD: an increase of ≥ 1.5 g/dL in Hb maintained for ≥ 16 consecutive weeks without any RBC transfusions for anemia; 2) LTB: no transfusions over ≥ 16 consecutive weeks; and 3) HTB: a reduction of $\geq 50\%$ in RBC units for ≥ 16 consecutive weeks. FAS: All subjects who signed the informed consent and received at least 1 dose of etavopivat. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.

End point type	Secondary
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End point timeframe:

48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[5]	0 ^[6]	0 ^[7]	
Units: Proportion of Subjects				
number (not applicable)				

Notes:

[5] - Data for this endpoint was not analysed and calculated due to early termination of study.

[6] - Data for this endpoint was not analysed due to early termination of study.

[7] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of all adverse events (AEs), serious adverse events (SAEs), and AEs related to etavopivat

End point title	Number of all adverse events (AEs), serious adverse events (SAEs), and AEs related to etavopivat
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End point description:

This endpoint was assessed for total number of AEs and SAEs in subjects, including AEs related to etavopivat. AEs are any unfavorable medical occurrences in subjects taking the medicinal product, regardless of causality. SAEs are severe AEs that result in death, are life-threatening, require hospitalization, lead to significant disability, or involve congenital anomalies. Important medical events posing risks to the subjects are also classified as SAEs. Treatment Emergent Adverse Events (TEAEs) are AEs occurring after treatment initiation, aiding in the safety assessment of etavopivat. TEAEs will be considered drug-related if assessed by the investigator as possibly related or related, or if relationship is missing. Safety population included all subjects who receive at least one dose of etavopivat (including partial dosing).

End point type	Secondary
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End point timeframe:

From baseline up to 48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	9	
Units: Events				
number (not applicable)				
AE	33	33	54	
SAE	1	0	6	
AEs related to etavopivat	0	0	1	
AEs possibly related etavopivat	8	3	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of premature discontinuations, dose interruptions, and dose reductions

End point title	Number of premature discontinuations, dose interruptions, and dose reductions
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End point description:

The endpoint was assessed for total number of premature discontinuations, dose interruptions and dose reductions. Premature discontinuation was defined as any discontinuation prior to week 48. A dose interruption is a temporary halt in treatment due to an AE, while a dose reduction involves lowering the dosage of the drug when AEs occur. If a subject tolerates a reduced dose for 14 days, a rechallenge with the original dose may occur after a clinic visit, but any new Grade 3 or higher AEs require treatment discontinuation and consultation with the Global Medical Monitor before resuming. Safety population included all subjects who receive at least one dose of etavopivat (including partial dosing).

End point type	Secondary
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End point timeframe:

Within 48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	9	
Units: Events				
number (not applicable)				
Premature discontinuations	1	0	0	
Dose interruptions	0	0	2	
Dose reductions	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response
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End point description:

This endpoint reported duration of response which was defined as duration of response will be summarized with quantiles based on product limit estimates (ie, Kaplan-Meier). Duration of response is defined as the time from date of first known incidence of a 2006 IWG criteria response to the most recent date that the 2006 IWG (International Working Group) criteria is not met following the initial response. If the subject has met IWG criteria throughout the period following the initial response, the subject will be censored at the latest date of end of study, loss to follow-up, or death. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.

End point type	Secondary
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End point timeframe:

Up to 48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[8]	0 ^[9]	0 ^[10]	
Units: Days				
number (not applicable)				

Notes:

[8] - Data for this endpoint was not analysed due to early termination of study.

[9] - Data for this endpoint was not analysed due to early termination of study.

[10] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate

End point title	Overall response rate
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End point description:

The Overall Response Rate (ORR) is defined as the proportion of subjects who achieve a predefined level of response according to the 2006 International Working Group (IWG) criteria, assessed at each scheduled evaluation. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.

End point type	Secondary
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End point timeframe:

Up to 48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[11]	0 ^[12]	0 ^[13]	
Units: Proportion of subjects				
number (not applicable)				

Notes:

[11] - Data for this endpoint was not analysed due to early termination of study.

[12] - Data for this endpoint was not analysed due to early termination of study.

[13] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in RBC transfusions for ≥ 8 weeks in subjects with LTD or HTB at study entry

End point title	Reduction in RBC transfusions for ≥ 8 weeks in subjects with LTD or HTB at study entry ^[14]
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End point description:

This endpoint reports reduction in RBC transfusion by 8-week interval in subjects with LTB and HTB. EES: All subjects in the FAS who have completed the week 24 response visit and who have a baseline record of the primary endpoint. n (number analysed) = subjects with available data for a specified category.

End point type	Secondary
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End point timeframe:

Up to 48 weeks

Notes:

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

Justification: Overall number of subjects analyzed signifies number of subjects evaluable for this outcome measure.

End point values	Low transfusion burden	High transfusion burden		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: Total RBS units				
arithmetic mean (standard deviation)				
Week 1-8 (n=2,4)	3.0 ($\pm$ 2.83)	5.8 ($\pm$ 2.63)		
Week 9-16 (n=2,4)	2.5 ($\pm$ 2.12)	6.3 ($\pm$ 1.71)		
Week 17-24 (n=2,4)	3.5 ($\pm$ 2.12)	7.5 ($\pm$ 3.00)		
Week 25-32 (n=2,3)	5.5 ($\pm$ 0.71)	7.3 ($\pm$ 1.15)		
Week 33-40 (n=2,3)	5.0 ($\pm$ 4.24)	6.7 ($\pm$ 1.15)		
Week 41-48 (n=2,2)	4.5 ($\pm$ 2.12)	7.5 ($\pm$ 2.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in RBC transfusion independence for ≥ 8 weeks in subjects with LTB or HTB at study entry

End point title	Percent Change from Baseline in RBC transfusion independence for ≥ 8 weeks in subjects with LTB or HTB at study entry ^[15]
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End point description:

This endpoint is percent change in RBC transfusion by 8-week interval in subjects with LTB and HTB. Percent reduction from baseline in RBC transfusion burden is defined as $-100 \times (\text{Total RBC Units Transfused During Interval}) / (\text{Baseline RBC Units Transfused Per 8 Weeks})$. EES: All subjects in the FAS who have completed the week 24 response visit and who have a baseline record of the primary endpoint. n (number analysed) = subjects with available data for a specified category. 99999 signifies the standard deviation was not evaluable.

End point type	Secondary
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End point timeframe:

Up to 48 weeks

Notes:

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

Justification: Overall number of subjects analyzed signifies number of subjects evaluable for this outcome measure.

End point values	Low transfusion burden	High transfusion burden		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: Percent change of total RBC units arithmetic mean (standard deviation)				
Week 1-8 (n=2,4)	-20.83 (± 64.818)	68.75 (± 156.994)		
Week 9-16 (n=2,4)	-33.33 (± 47.140)	68.75 (± 98.219)		
Week 17-24 (n=2,4)	-4.17 (± 41.248)	120.83 (± 191.183)		
Week 25-32 (n=2,3)	58.33 (± 11.785)	127.78 (± 149.381)		
Week 33-40 (n=2,3)	33.33 (± 94.281)	94.44 (± 91.793)		
Week 41-48 (n=2,2)	25.00 (± 35.355)	50.00 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in neutrophils and/or platelets counts

End point title	Change from baseline in neutrophils and/or platelets counts
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End point description:

This endpoint reports the change from baseline in neutrophils and/or platelets counts from baseline to week 48. The safety set includes all subjects who receive at least one dose of etavopivat (including partial dosing). Here, n (number analysed) = subjects with available data for a specified category. 99999 signifies the standard deviation was not evaluable.

End point type	Secondary
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End point timeframe:

Baseline (week 0), week 48

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	9	
Units: Giga per liter (10 ⁹ /L)				
arithmetic mean (standard deviation)				
Neutrophils (n=1,2,1)	-3.200 (± 99999)	-0.950 (± 0.0707)	-0.100 (± 99999)	
Platelets counts (n=1,2,1)	43.0 (± 99999)	-51.0 (± 205.06)	-8.0 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Decrease in ferritin and transferrin saturation (TSAT)

End point title	Decrease in ferritin and transferrin saturation (TSAT)
End point description:	
This endpoint were to report decrease in ferritin and TSAT from baseline to Week 48. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.	
End point type	Secondary
End point timeframe:	
Up to 48 weeks	

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[16]	0 ^[17]	0 ^[18]	
Units: ng/mL				
number (not applicable)				

Notes:

[16] - Data for this endpoint was not analysed due to early termination of study.

[17] - Data for this endpoint was not analysed due to early termination of study.

[18] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Decrease in iron chelation therapy

End point title	Decrease in iron chelation therapy
End point description:	
This endpoint was expected to report decrease of Iron chelation therapy recorded throughout the study. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.	
End point type	Secondary
End point timeframe:	
up to 48 weeks	

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[19]	0 ^[20]	0 ^[21]	
Units: Dose unit				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[19] - Data for this endpoint was not analysed due to early termination of study.

[20] - Data for this endpoint was not analysed due to early termination of study.

[21] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
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End point description:

Overall survival is defined as the time from first dose to date of death. If the subject was alive at last contact, the end date will be censored at the latest of either end of study, loss to follow-up, or study discontinuation. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.

End point type	Secondary
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End point timeframe:

Within 48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[22]	0 ^[23]	0 ^[24]	
Units: Months				
number (not applicable)				

Notes:

[22] - Data for this endpoint was not analysed due to early termination of study.

[23] - Data for this endpoint was not analysed due to early termination of study.

[24] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Etavopivat plasma concentrations

End point title	Etavopivat plasma concentrations
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End point description:

This endpoint reported Etavopivat plasma concentrations in order to assess the PK properties of etavopivat in subjects with MDS. PK parameters included but not limited to were: Time to maximum

observed plasma concentration, area under the plasma concentration-time curve from time zero until the last quantifiable time point (AUC0-last), from time zero to infinity (AUC0-inf), for a dosing interval (AUCtau/AUC0-24).) However due to early termination of the study, all the PK parameters could not be assessed and only the plasma concentrations was assessed. The PK set includes all safety set subjects who have at least one evaluable concentration for etavopivat at a scheduled PK time point after the start of dosing. Here, n (number analysed) = subjects with available data for a specified category. 99999 signifies the arithmetic mean and standard deviation was not evaluable.

End point type	Secondary
End point timeframe:	
Weeks 1 and 4 pre-dose, post-dose 1, 2, 4, 6 hours. Week 2 and EOT (week 48): pre-dose, post-dose 1, 2 hours	

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	9	
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Week 1 predose (n=3,4,9)	0 (± 99999)	0 (± 99999)	0 (± 99999)	
Week 1 post-dose 1 hour (n=3,5,9)	379.77 (± 292.748)	904.80 (± 521.000)	1016.78 (± 794.503)	
Week 1 post-dose 2 hour (n=3,5,9)	751.67 (± 393.465)	579.60 (± 403.593)	519.11 (± 273.776)	
Week 1 post-dose 4 hour (n=2,5,9)	274.50 (± 86.974)	203.80 (± 134.884)	165.16 (± 64.895)	
Week 1 post-dose 6 hour (n=1,5,7)	63.50 (± 99999)	101.02 (± 67.693)	83.74 (± 40.170)	
Week 2 pre-dose (n=3,4,9)	27.20 (± 17.843)	19.08 (± 9.037)	19.20 (± 12.240)	
Week 2 post-dose 1 hour (n=3,5,9)	1156.00 (± 371.198)	899.40 (± 442.555)	1076.44 (± 693.907)	
Week 2 post-dose 2 hour (n=3,4,9)	927.00 (± 310.140)	1024.00 (± 530.102)	661.78 (± 392.238)	
Week 4 predose (n=2,5,9)	17.04 (± 11.540)	24.34 (± 23.333)	20.26 (± 9.289)	
Week 4 post-dose 1 hour (n=2,4,9)	1050.00 (± 28.284)	386.90 (± 214.249)	913.20 (± 1013.207)	
Week 4 post-dose 2 hour (n=2,5,9)	526.00 (± 134.350)	453.40 (± 179.140)	678.49 (± 379.918)	
Week 4 post-dose 4 hour (n=2,4,9)	151.50 (± 12.021)	383.73 (± 261.103)	297.90 (± 282.646)	
Week 4 post-dose 6 hour (n=2,3,9)	60.75 (± 11.526)	148.13 (± 113.650)	121.34 (± 115.306)	
End of treatment pre-dose (n=0,2,1)	99999 (± 99999)	21.60 (± 5.798)	24.20 (± 99999)	
End of treatment post-dose 1 hours (n=0,1,1)	99999 (± 99999)	1620.00 (± 99999)	1680.00 (± 99999)	
End of treatment post-dose 2 hours (n=0,1,1)	99999 (± 99999)	571.00 (± 99999)	815.00 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: RBC 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP) levels over time

End point title	RBC 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP) levels over time
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End point description:

Etavopivat plasma concentrations were collected in order to assess the pharmacodynamic (PD) properties of etavopivat in subjects with MDS. Data for this endpoint were not evaluable due to low subject enrolment and early termination of study.

End point type	Secondary
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End point timeframe:

Within 48 weeks

End point values	Non-transfusion dependent	Low transfusion burden	High transfusion burden	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[25]	0 ^[26]	0 ^[27]	
Units: Micrograms per milliliter				
number (not applicable)				

Notes:

[25] - Data for this endpoint was not analysed due to early termination of study.

[26] - Data for this endpoint was not analysed due to early termination of study.

[27] - Data for this endpoint was not analysed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 48 weeks

Adverse event reporting additional description:

All presented AEs are treatment emergent AEs (TEAE). TEAE is defined as any AE that emerges or worsens in the period from first dose of study drug to 28 days after the last dose of study drug. Safety population includes all subjects who receive at least one dose of etavopivat (including partial dosing).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25
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Reporting groups

Reporting group title	Non-transfusion dependent
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Reporting group description:

Non transfusion dependent participants who had received less than equal to ≤ 2 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Reporting group title	High transfusion burden
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Reporting group description:

High transfusion burden participants who had received greater than equal ≥ 8 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Reporting group title	Low transfusion burden
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Reporting group description:

Low transfusion burden participants who had received 3 to 7 RBC transfusions for anaemia within the prior 16 weeks, orally received 400 mg of etavopivat once daily for up to 48 weeks.

Serious adverse events	Non-transfusion dependent	High transfusion burden	Low transfusion burden
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	3 / 9 (33.33%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Arterial rupture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Non-transfusion dependent	High transfusion burden	Low transfusion burden
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	9 / 9 (100.00%)	5 / 5 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Mucosal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 3 (66.67%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Cough			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 3 (66.67%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Depression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 9 (22.22%)	0 / 5 (0.00%)
occurrences (all)	1	3	0

Investigations			
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 3	0 / 5 (0.00%) 0
Lymphocyte count decreased subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 3	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Lipase increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 5 (20.00%) 2
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 5 (20.00%) 10
Troponin I increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 4	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Injury, poisoning and procedural complications			
Hip fracture subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Transfusion reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Cardiac disorders			

Cardiac failure subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1
Atrioventricular block second degree subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 9 (22.22%) 3	0 / 5 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 3	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0
Ear and labyrinth disorders External ear inflammation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 9 (22.22%) 2	0 / 5 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1

Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	1 / 5 (20.00%)
occurrences (all)	0	3	1
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Pain in extremity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1
Infections and infestations			
Cellulitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	1 / 5 (20.00%) 1
Herpes zoster subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Eye infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Ear infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1
Lip infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Skin infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	2 / 5 (40.00%) 2
Metabolism and nutrition disorders			

Haemosiderosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Iron overload			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypervolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 5 (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
11 April 2022	Version 1.0: First protocol version
15 June 2022	Version 2.0: Protocol version 1.0 was not implemented.
31 July 2023	Version 3.0: 1. Protocol version updated to adjust the treatment period timeframes into a 24-week Primary Treatment period, a 24-week Extension Treatment period, and a Survival Follow-up period. 2. A 'futility assessment' was added. 3. Schedule of Events tables and Appendices were updated as needed to reflect the above changes to the protocol. 4. Safety text has been added throughout the document to reflect the Novo Nordisk Safety Surveillance practice.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The predefined Quality Tolerance Limit (QTL) that required 5 or more subjects to complete 16 weeks of treatment. However, 7 subjects did not fulfill this requirement, leading to the early termination.
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Notes: