



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multiple-dose Phase 2 Study to Evaluate the Efficacy and Safety of BMS-986263 in Adults with Compensated Cirrhosis from Nonalcoholic Steatohepatitis (NASH)

Summary

EudraCT number	2019-003932-22
Trial protocol	FR BE DE IT NL
Global end of trial date	09 February 2024

Results information

Result version number	v1 (current)
This version publication date	28 August 2024
First version publication date	28 August 2024

Trial information

Trial identification

Sponsor protocol code	IM025-017
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	09 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of BMS-986263 compared with placebo to improve liver fibrosis in participants with compensated cirrhosis due to NASH

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 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	Israel: 2
Country: Number of subjects enrolled	Japan: 18
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	United States: 52
Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Brazil: 10
Worldwide total number of subjects	124
EEA total number of subjects	24

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)	88
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

124 Subjects Randomized 122 Treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

Placebo

Arm title	Treatment 1
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Arm description:

BMS-986263 45mg QW

Arm type	Experimental
Investigational medicinal product name	BMS-986263
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg per vial; 3 mg/mL

Arm title	Treatment 2
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Arm description:

BMS-986263 90mg QW

Arm type	Experimental
Investigational medicinal product name	BMS-986263
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg per vial; 3 mg/mL

Number of subjects in period 1	Placebo	Treatment 1	Treatment 2
Started	40	42	42
Completed	39	41	42
Not completed	1	1	0
Adverse event, non-fatal	1	-	-
Administrative Reasons by Sponsor	-	1	-

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

Placebo

Arm title	Treatment 1
------------------	-------------

Arm description:

BMS-986263 45mg QW

Arm type	Experimental
Investigational medicinal product name	BMS-986263
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg per vial; 3 mg/mL

Arm title	Treatment 2
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Arm description:

BMS-986263 90mg QW

Arm type	Experimental
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Investigational medicinal product name	BMS-986263
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg per vial; 3 mg/mL

Number of subjects in period 2	Placebo	Treatment 1	Treatment 2
Started	39	41	42
Completed	36	35	35
Not completed	3	6	7
Adverse event, non-fatal	-	2	3
Participant Withdrew Consent	-	-	1
Administrative Reasons by Sponspor	3	4	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Treatment 1
Reporting group description: BMS-986263 45mg QW	
Reporting group title	Treatment 2
Reporting group description: BMS-986263 90mg QW	

Reporting group values	Placebo	Treatment 1	Treatment 2
Number of subjects	40	42	42
Age categorical Units: Subjects			
Adults (18-64 years)	31	32	25
From 65-84 years	9	10	17
Age Continuous Units: Years			
arithmetic mean	58.9	58.9	60.0
standard deviation	± 8.56	± 6.76	± 8.65
Sex: Female, Male Units: Participants			
Female	22	25	25
Male	18	17	17
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	6	11	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	34	31	32
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	22	13	18
Not Hispanic or Latino	7	18	17
Unknown or Not Reported	11	11	7

Reporting group values	Total		
Number of subjects	124		
Age categorical Units: Subjects			
Adults (18-64 years)	88		
From 65-84 years	36		

Age Continuous Units: Years arithmetic mean standard deviation	-		
Sex: Female, Male Units: Participants			
Female	72		
Male	52		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	26		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	97		
More than one race	0		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	53		
Not Hispanic or Latino	42		
Unknown or Not Reported	29		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Treatment 1
Reporting group description: BMS-986263 45mg QW	
Reporting group title	Treatment 2
Reporting group description: BMS-986263 90mg QW	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Treatment 1
Reporting group description: BMS-986263 45mg QW	
Reporting group title	Treatment 2
Reporting group description: BMS-986263 90mg QW	

Primary: Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (NASH CRN Fibrosis Score), as determined by liver biopsy after 12 weeks of treatment.

End point title	Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (NASH CRN Fibrosis Score), as determined by liver biopsy after 12 weeks of treatment. ^[1]
End point description: Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (NASH CRN Fibrosis Score), as determined by liver biopsy after 12 weeks of treatment. For the NASH CRN Fibrosis Score, fibrosis is staged on a 0 to 4 scale: 0 (none); 1 (perisinusoidal or periportal fibrosis); 2 (perisinusoidal and portal/periportal fibrosis); 3 (bridging fibrosis); 4 (cirrhosis).	
End point type	Primary
End point timeframe: 12 Weeks	

Notes:

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

Justification: No Statistical Analysis done for this endpoint

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Percentage				
number (not applicable)				
responders	20.5	12.2	7.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (NASH CRN Fibrosis Score) with no worsening of NASH after 12 weeks of treatment.

End point title	Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (NASH CRN Fibrosis Score) with no worsening of NASH after 12 weeks of treatment.
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End point description:

Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (NASH CRN Fibrosis Score) with no worsening of NASH after 12 weeks of treatment.

For the NASH CRN Fibrosis Score, fibrosis is staged on a 0 to 4 scale: 0 (none); 1 (perisinusoidal or periportal fibrosis); 2 (perisinusoidal and portal/periportal fibrosis); 3 (bridging fibrosis); 4 (cirrhosis).

End point type	Secondary
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End point timeframe:

12 Weeks

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Percentage				
number (not applicable)				
responders	20.5	12.2	4.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve ≥ 2 stage improvement in liver fibrosis (NASH CRN Fibrosis Score) with no worsening of NASH after 12 weeks of treatment.

End point title	Percentage of participants who achieve ≥ 2 stage improvement in liver fibrosis (NASH CRN Fibrosis Score) with no worsening of NASH after 12 weeks of treatment.
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End point description:

Percentage of participants who achieve ≥ 2 stage improvement in liver fibrosis (NASH CRN Fibrosis Score) with no worsening of NASH after 12 weeks of treatment.

For the NASH CRN Fibrosis Score, fibrosis is staged on a 0 to 4 scale: 0 (none); 1 (perisinusoidal or periportal fibrosis); 2 (perisinusoidal and portal/periportal fibrosis); 3 (bridging fibrosis); 4 (cirrhosis).

End point type	Secondary
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End point timeframe:

12 Weeks

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Percentage				
number (not applicable)				
responders	2.6	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (modified Ishak score) after 12 weeks of treatment.

End point title	Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (modified Ishak score) after 12 weeks of treatment.
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End point description:

Percentage of participants who achieve ≥ 1 stage improvement in liver fibrosis (modified Ishak score) after 12 weeks of treatment.

A modified Ishak scoring system (0 to 6 scale) was originally developed to grade portal-based liver fibrosis associated with viral hepatitis. The modified Ishak system has been adapted to grade central-based liver fibrosis associated with NASH, and it also uses a 0 to 6 scale:

0: No fibrosis

1: perisinusoidal or periportal fibrosis

2: perisinusoidal and portal/periportal fibrosis

3: bridging fibrosis with linkage of $< 50\%$ of vascular structures (portal and centrilobular)

4: bridging fibrosis with linkage of $> 50\%$ of vascular structures (portal and centrilobular)

5: early or incomplete cirrhosis

6: established or advanced cirrhosis

End point type	Secondary
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End point timeframe:

12 Weeks

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Percentage				
number (not applicable)				
Responders	30.8	26.8	21.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve ≥ 2 stage improvement in liver fibrosis (modified Ishak score) after 12 weeks of treatment.

End point title	Percentage of participants who achieve ≥ 2 stage improvement in liver fibrosis (modified Ishak score) after 12 weeks of treatment.
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End point description:

Percentage of participants who achieve ≥ 2 stage improvement in liver fibrosis (modified Ishak score) after 12 weeks of treatment.

A modified Ishak scoring system (0 to 6 scale) was originally developed to grade portal-based liver fibrosis associated with viral hepatitis. The modified Ishak system has been adapted to grade central-based liver fibrosis associated with NASH, and it also uses a 0 to 6 scale:

0: No fibrosis

1: perisinusoidal or periportal fibrosis

2: perisinusoidal and portal/periportal fibrosis

3: bridging fibrosis with linkage of $< 50\%$ of vascular structures (portal and centrilobular)

4: bridging fibrosis with linkage of $> 50\%$ of vascular structures (portal and centrilobular)

5: early or incomplete cirrhosis

6: established or advanced cirrhosis

End point type	Secondary
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End point timeframe:

12 Weeks

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Percentage				
number (not applicable)				
responders	10.3	4.9	4.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in CPA after 12 weeks of Treatment

End point title	Mean change from baseline in CPA after 12 weeks of Treatment
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End point description:

Change from baseline in CPA after 12 weeks of treatment.

Assessment of collagen proportionate area (CPA) is a method by which the amount (percentage) of collagen in stained tissue sections is analyzed using morphometric image analysis. This allows for a quantitative assessment of fibrosis. Percentage of fat in stained tissue sections is also analyzed using morphometric image analysis.

End point type	Secondary
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End point timeframe:

12 Weeks

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	32	27	
Units: Percentage				
arithmetic mean (standard error)	-3.67 (± 1.861)	-0.35 (± 1.374)	-3.67 (± 1.973)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAE) and Treatment Emergent Serious Adverse Events (TESAE)

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAE) and Treatment Emergent Serious Adverse Events (TESAE)
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End point description:

An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study drug and that does have a causal relationship with this treatment.

End point type	Secondary
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End point timeframe:

From First Treatment to end of Follow up (36 weeks)

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Participants				
TEAE	24	33	34	
TESAE	1	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with clinically significant changes in clinical laboratory values.

End point title	Number of Participants with clinically significant changes in clinical laboratory values.
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End point description:

Investigators must document their review of each laboratory safety report. A central laboratory will perform the analyses and will provide reference ranges for these tests.

clinical laboratory assessments analyzed:
Hematology, Blood Chemistry, Urinalysis and a Metabolic Panel.

End point type	Secondary
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End point timeframe:

From First Treatment to end of Follow up (36 weeks)

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with clinically significant changes in vitals signs.

End point title	Number of Participants with clinically significant changes in vitals signs.
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End point description:

Includes body temperature, respiratory rate, blood pressure, and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.

End point type	Secondary
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End point timeframe:

From First Treatment to end of Follow up (36 weeks)

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with clinically significant changes in physical examination findings.

End point title	Number of Participants with clinically significant changes in physical examination findings.
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End point description:

Physical examination includes body weight, height, and BMI (height and BMI calculation at screening only).

End point type	Secondary
End point timeframe:	
From First Treatment to end of Follow up (36 weeks)	

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with clinically significant changes in electrocardiogram readings.

End point title	Number of Participants with clinically significant changes in electrocardiogram readings.
End point description:	
Number of Participants with clinically significant changes in electrocardiogram readings.	
End point type	Secondary
End point timeframe:	
From First Treatment to end of Follow up (36 weeks)	

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with clinically significant changes in BMD.

End point title	Number of Participants with clinically significant changes in BMD.
End point description:	
Bone Mineral Density(BMD) will be measured by a dual-energy X-ray absorptiometry (DXA) Scan.	
End point type	Secondary
End point timeframe:	
From First Treatment to end of Follow up (36 weeks)	

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	41	42	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of BMS-986263 components at the end of 12 weeks.

End point title	Plasma Concentration of BMS-986263 components at the end of 12 weeks.
End point description:	Plasma concentrations of BMS-986263 components siRNA, DPD, HEDC, and S104.
End point type	Secondary
End point timeframe:	From First Treatment to end of Follow up (36 weeks)

End point values	Placebo	Treatment 1	Treatment 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	42	42	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
siRNA	()	38.9 (± 151)	72.9 (± 169)	
DPD	()	519 (± 45.2)	1138 (± 80.7)	
HEDC	()	25.1 (± 51.8)	59.0 (± 58.8)	
S104	()	4.16 (± 141)	3.68 (± 50.7)	

Notes:

[2] - Subjects in this arm not given treatment drug to have components

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events: (From first dose to last dose + 24 week follow up):
Approximately 36 Weeks

All-Cause mortality (From randomization to end of study): Approximately 42 Weeks.

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	PLACEBO
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Reporting group description:

Placebo

Reporting group title	Treatment 2
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Reporting group description:

BMS-986263 90mg QW

Reporting group title	Treatment 1
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Reporting group description:

BMS-986263 45mg QW

Serious adverse events	PLACEBO	Treatment 2	Treatment 1
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 39 (2.56%)	2 / 42 (4.76%)	1 / 41 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	1 / 39 (2.56%)	0 / 42 (0.00%)	0 / 41 (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
Post procedural haematoma			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 41 (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
Procedural complication			

subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 41 (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
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 41 (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
Infections and infestations			
Infected cyst			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	PLACEBO	Treatment 2	Treatment 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 39 (43.59%)	29 / 42 (69.05%)	24 / 41 (58.54%)
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 39 (0.00%)	22 / 42 (52.38%)	17 / 41 (41.46%)
occurrences (all)	0	70	44
Procedural pain			
subjects affected / exposed	2 / 39 (5.13%)	1 / 42 (2.38%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 39 (10.26%)	6 / 42 (14.29%)	4 / 41 (9.76%)
occurrences (all)	6	12	13
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Fatigue			

subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	4 / 42 (9.52%) 15	1 / 41 (2.44%) 1
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	2 / 39 (5.13%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Nausea			
subjects affected / exposed	3 / 39 (7.69%)	1 / 42 (2.38%)	2 / 41 (4.88%)
occurrences (all)	5	1	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 39 (5.13%)	1 / 42 (2.38%)	1 / 41 (2.44%)
occurrences (all)	2	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 39 (5.13%)	2 / 42 (4.76%)	2 / 41 (4.88%)
occurrences (all)	2	2	2
Back pain			
subjects affected / exposed	2 / 39 (5.13%)	2 / 42 (4.76%)	2 / 41 (4.88%)
occurrences (all)	2	3	2
Muscle spasms			
subjects affected / exposed	3 / 39 (7.69%)	1 / 42 (2.38%)	1 / 41 (2.44%)
occurrences (all)	3	1	1
Myalgia			
subjects affected / exposed	4 / 39 (10.26%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	7	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 39 (10.26%)	1 / 42 (2.38%)	4 / 41 (9.76%)
occurrences (all)	4	1	4
Urinary tract infection			
subjects affected / exposed	2 / 39 (5.13%)	1 / 42 (2.38%)	0 / 41 (0.00%)
occurrences (all)	2	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2022	<p>The primary purpose of this Global Revised Protocol is to expand the patient population from Child-Pugh A5 to Child-Pugh A6, including corresponding laboratory exclusion criteria, based on preliminary results from hepatic impairment (HI) study IM025015. Key secondary revisions include the following:</p> <ul style="list-style-type: none">Adding results from Part 1 of HI study IM025015, which supports the changes in Child-Pugh/laboratory exclusion criteriaAdjustment of step-wise infusion rates (decreased number of steps)Adding a ({Bis[2-(tetradecanoyloxy)ethyl] carbamoyl}methyl)-(2-hydroxyethyl)dimethylazanium bromide (HEDC; lipid component) assayAdding guidance and exploratory assessments related to the coronavirus disease 2019 (COVID-19) pandemicChanging statistical sample size calculation, study stratification factors, and statistical analysis methodology for primary endpointExcluding participants from the study who are taking anticoagulantsReplacing liver ultrasound as a screening procedure for detection of hepatocellular carcinoma (HCC) with multiphasic liver computed tomography (CT)/magnetic resonance imaging (MRI)Updating exclusion criterion related to history of weight gain/lossUpdating exclusion criterion related to history of illegal intravenous (IV) drug useAdding option for participants who have a prolonged international normalized ratio (INR) and/or lower platelet count to potentially receive treatments for coagulation abnormalities and/or low platelet counts prior to liver biopsy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported