# 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 |

**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 |
| **Arm title** | Placebo |

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 |

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 |
| **Arm title** | Placebo |
| 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 |
| 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 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<br>Units: Subjects | | | |
| Adults (18-64 years) | 31 | 32 | 25 |
| From 65-84 years | 9 | 10 | 17 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 58.9 | 58.9 | 60.0 |
| standard deviation | ± 8.56 | ± 6.76 | ± 8.65 |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 22 | 25 | 25 |
| Male | 18 | 17 | 17 |
| Race (NIH/OMB)<br>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)<br>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<br>Units: Subjects | | | |
| Adults (18-64 years) | 88 | | |
| From 65-84 years | 36 | | |

| | | | |
|---|---|---|---|
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | <br><br><br>- | | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 72 | | |
| Male | 52 | | |
| Race (NIH/OMB)<br>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)<br>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. |
|---|---|

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 |
|---|---|

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. |
|---|---|

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 |
|---|---|

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. |
|---|---|

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 tograde 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 |
|---|---|

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. |
|---|---|

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 tograde 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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) |
|---|---|

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 |
|---|---|

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. |
|---|---|

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 |
|---|---|

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. |
|---|---|

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 |
|---|---|

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. |
|---|---|

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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 26.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | PLACEBO |
| Reporting group description: | |
| Placebo | |
| Reporting group title | Treatment 2 |
| Reporting group description: | |
| BMS-986263 90mg QW | |
| Reporting group title | Treatment 1 |
| 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 | 2 / 39 (5.13%) | 4 / 42 (9.52%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 15 | 1 |
| Gastrointestinal disorders | | | |
| Gastrooesophageal 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 | The primary purpose of this Global Revised Protocol is to expand the patient population from<br>Child-Pugh A5 to Child-Pugh A6, including corresponding laboratory exclusion criteria, based on<br>preliminary results from hepatic impairment (HI) study IM025015. Key secondary revisions<br>include the following:<br>Adding results from Part 1 of HI study IM025015, which supports the changes in Child-<br>Pugh/laboratory exclusion criteria<br>Adjustment of step-wise infusion rates (decreased number of steps)<br>Adding a ({Bis[2-(tetradecanoyloxy)ethyl] carbamoyl}methyl)-(2-hydroxyethyl)dimethylazanium bromide (HEDC; lipid component) assay<br>Adding guidance and exploratory assessments related to the coronavirus disease 2019<br>(COVID-19) pandemic<br>Changing statistical sample size calculation, study stratification factors, and statistical<br>analysis methodology for primary endpoint<br>Excluding participants from the study who are taking anticoagulants<br>Replacing liver ultrasound as a screening procedure for detection of hepatocellular carcinoma<br>(HCC) with multiphasic liver computed tomography (CT)/magnetic resonance imaging<br>(MRI)<br>Updating exclusion criterion related to history of weight gain/loss<br>Updating exclusion criterion related to history of illegal intravenous (IV) drug use<br>Adding option for participants who have a prolonged international normalized ratio (INR)<br>and/or lower platelet count to potentially receive treatments for coagulation abnormalities<br>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