



Clinical trial results:

A Phase II/III seamless, randomised, double-blind, placebo-controlled, parallel-group, group-sequential study to evaluate efficacy, safety and tolerability of BI 767551 for the treatment of symptomatic, non-hospitalized adults with mild to moderate COVID-19

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2020-005588-29 |
| Trial protocol | BE DK NL PT DE ES |
| Global end of trial date | 04 October 2021 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 14 July 2022 |
| First version publication date | 14 July 2022 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 1487-0001 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04822701 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216 |
| Public contact | Boehringer Ingelheim Call Center, Boehringer Ingelheim, +1 18002430127, clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | Boehringer Ingelheim Call Center, Boehringer Ingelheim, +1 18002430127, clintriage.rdg@boehringer-ingelheim.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 | 16 November 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 July 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 October 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the concept of pharmacological activity of BI 767551 in non-hospitalised patients with mild to moderate COVID-19 symptoms and to identify a potentially efficacious and safe dose regimen from the Phase II part to take into the Phase III part. To evaluate the efficacy, safety, and tolerability of BI 767551 for the treatment of symptomatic, non-hospitalised adults with mild to moderate COVID-19.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 17 June 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 | Spain: 1 |
| Country: Number of subjects enrolled | United States: 6 |
| Worldwide total number of subjects | 7 |
| EEA total number of subjects | 1 |

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) | 7 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

This study was planned to evaluate the concept of pharmacological activity of BI 767551 in non-hospitalised patients with mild to moderate COVID-19 symptoms. The study was terminated early. 5 patients total participated in phase II and phase III was not conducted.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Randomised |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Blinding implementation details:

Patients, investigators, central reviewers, and everyone involved in trial conduct with exception of the pharmacist will remain double-blind with regard to the randomised treatment assignments.

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo intravenous (i.v.) + placebo inhaled |

Arm description:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion.

| | |
|--|-----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Solvent for BI 767551 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solvent for solution for infusion |
| Routes of administration | Inhalation use |

Dosage and administration details:

A single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Sterile normal saline (NaCl 0.9%) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes on Day 1

| | |
|------------------|---|
| Arm title | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
|------------------|---|

Arm description:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start

approximately 25 min after the start of infusion.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BI 767551 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

A single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Sterile normal saline (NaCl 0.9%) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes on Day 1

| Number of subjects in period 1 | Placebo intravenous (i.v.) + placebo inhaled | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
|--------------------------------|--|---|
| Started | 4 | 1 |
| Completed | 2 | 1 |
| Not completed | 2 | 0 |
| Not treated | 2 | - |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Treated |
| Is this the baseline period? | Yes ^[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo intravenous (i.v.) + placebo inhaled |

Arm description:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Solvent for BI 767551 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solvent for solution for infusion |
| Routes of administration | Inhalation use |

Dosage and administration details:

A single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Sterile normal saline (NaCl 0.9%) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes on Day 1

| | |
|------------------|---|
| Arm title | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
|------------------|---|

Arm description:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion.

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BI 767551 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

A single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Sterile normal saline (NaCl 0.9%) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes on Day 1

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The baseline characteristics were analyzed using treated participants.

| Number of subjects in period 2^[2] | Placebo intravenous (i.v.) + placebo inhaled | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
|---|--|---|
| Started | 2 | 1 |
| Completed | 0 | 1 |
| Not completed | 2 | 0 |
| Consent withdrawn by subject | 1 | - |
| Lost to follow-up | 1 | - |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups

| | |
|--|---|
| Reporting group title | Placebo intravenous (i.v.) + placebo inhaled |
| Reporting group description: | |
| Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion. | |
| Reporting group title | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
| Reporting group description: | |
| Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion. | |

| Reporting group values | Placebo intravenous (i.v.) + placebo inhaled | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled | Total |
|---|--|---|-------|
| Number of subjects | 2 | 1 | 3 |
| Age categorical | | | |
| Treated set (TS): This subject set includes all subjects who received any amount of study drug. | | | |
| 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) | 2 | 1 | 3 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Treated set (TS): This subject set includes all subjects who received any amount of study drug. The "9999" stands for "not applicable". | | | |
| Units: years | | | |
| arithmetic mean | 35.5 | 37.0 | |
| standard deviation | ± 10.6 | ± 9999 | - |
| Sex: Female, Male | | | |
| Treated set (TS): This subject set includes all subjects who received any amount of study drug. | | | |
| Units: Participants | | | |
| Female | 2 | 1 | 3 |
| Male | 0 | 0 | 0 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |

| | | | |
|--|--------|--------|---|
| Black or African American | 0 | 0 | 0 |
| White | 2 | 1 | 3 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Treated set (TS): This subject set includes all subjects who received any amount of study drug. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 2 | 0 | 2 |
| Not Hispanic or Latino | 0 | 1 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Log-transformed Nasopharyngeal (NP) swab viral load at baseline | | | |
| Each viral load result indicates the number of virus copies in a milliliter, and the raw values were log-transformed, resulting in log10 viral load. The "9999" stands for "not applicable". | | | |
| Units: Log-transformed copies / milliliter | | | |
| arithmetic mean | 5.24 | 7.32 | |
| standard deviation | ± 2.09 | ± 9999 | - |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Placebo intravenous (i.v.) + placebo inhaled |
| Reporting group description: Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion. | |
| Reporting group title | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
| Reporting group description: Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion. | |
| Reporting group title | Placebo intravenous (i.v.) + placebo inhaled |
| Reporting group description: Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion. | |
| Reporting group title | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
| Reporting group description: Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion. | |

Primary: Phase II: Time-weighted change from baseline in viral shedding over 8 days in site collected nasopharyngeal (NP) swabs by Quantitative Reverse Transcription Polymerase chain reaction (RT-qPCR)

| | |
|---|---|
| End point title | Phase II: Time-weighted change from baseline in viral shedding over 8 days in site collected nasopharyngeal (NP) swabs by Quantitative Reverse Transcription Polymerase chain reaction (RT-qPCR) ^[1] |
| End point description: Time-weighted change from baseline in viral shedding over 8 days in site collected nasopharyngeal (NP) swabs by Quantitative Reverse Transcription Polymerase chain reaction (RT-qPCR), defined as a absolute change from baseline in log10 viral load, is reported. The "9999" stands for "not applicable". Modified Intention-To-Treat set (mITT): This subject set includes all randomised subjects that received any amount of study drug and who have at least a measurable baseline value (above Lower limit of quantification (LLOQ)) and a second measurement in the first week (up to 7 days after drug intake) of SARS-CoV-2 RNA by site collected nasopharyngeal (NP) swab. | |
| End point type | Primary |
| End point timeframe: Up to 8 days | |

Notes:

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

Justification: The endpoint was planned to explore descriptively.

| End point values | Placebo intravenous (i.v.) + placebo inhaled | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled | | |
|--|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 1 ^[2] | | |
| Units: Log-transformed copies / milliliter | | | | |
| arithmetic mean (standard deviation) | 0.15 (± 1.25) | -2.84 (± 9999) | | |

Notes:

[2] - "9999" stands for "not applicable".

Statistical analyses

No statistical analyses for this end point

Primary: Phase II: Time-weighted change from baseline in viral shedding over 29 days in site collected nasopharyngeal (NP) swabs by Quantitative Reverse Transcription Polymerase chain reaction (RT-qPCR)

| | |
|-----------------|--|
| End point title | Phase II: Time-weighted change from baseline in viral shedding over 29 days in site collected nasopharyngeal (NP) swabs by Quantitative Reverse Transcription Polymerase chain reaction (RT-qPCR) ^[3] |
|-----------------|--|

End point description:

Time-weighted change from baseline in viral shedding over 29 days in site collected nasopharyngeal (NP) swabs by Quantitative Reverse Transcription Polymerase chain reaction (RT-qPCR), defined as a absolute change from baseline in log10 viral load, is reported. The "9999" stands for "not applicable".

Modified Intention-To-Treat set (mITT): This subject set includes all randomised subjects that received any amount of study drug and who have at least a measurable baseline value (above Lower limit of quantification (LLOQ)) and a second measurement in the first week (up to 7 days after drug intake) of SARS-CoV-2 RNA by site collected nasopharyngeal (NP) swab.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 29 days

Notes:

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

Justification: The endpoint was planned to explore descriptively.

| End point values | Placebo intravenous (i.v.) + placebo inhaled | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled | | |
|--|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 1 ^[4] | | |
| Units: Log-transformed copies / milliliter | | | | |
| arithmetic mean (standard deviation) | -2.09 (± 1.60) | -4.18 (± 9999) | | |

Notes:

[4] - "9999" stands for "not applicable".

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Number of participants with loss of detection of Severe acute respiratory syndrome coronavirus 2 ribonucleic acid (SARS-CoV-2 RNA) by site collected NP swab at Day 4, 8, 15, 22 and 29

| | |
|-----------------|---|
| End point title | Phase II: Number of participants with loss of detection of Severe acute respiratory syndrome coronavirus 2 ribonucleic acid (SARS-CoV-2 RNA) by site collected NP swab at Day 4, 8, 15, 22 and 29 |
|-----------------|---|

End point description:

Number of participants with loss of detection of Severe acute respiratory syndrome coronavirus 2 ribonucleic acid (SARS-CoV-2 RNA) by site collected NP swab at Day 4, 8, 15, 22 and 29 is report. The "Yes" = loss of detection of SARS-CoV-2 RNA; "No" = SARS-CoV-2 RNA detected; "Missing" = not evaluable.

Treated set (TS): This subject set includes all subjects who received any amount of study drug.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 4, Day 8, Day 15, Day 22, and Day 29

| End point values | Placebo intravenous (i.v.) + placebo inhaled | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 1 | | |
| Units: Participants | | | | |
| Day 4 Yes | 0 | 0 | | |
| Day 4 No | 2 | 1 | | |
| Day 4 Missing | 0 | 0 | | |
| Day 8 Yes | 0 | 0 | | |
| Day 8 No | 2 | 1 | | |
| Day 8 Missing | 0 | 0 | | |
| Day 15 Yes | 1 | 1 | | |
| Day 15 No | 1 | 0 | | |
| Day 15 Missing | 0 | 0 | | |
| Day 22 Yes | 1 | 0 | | |
| Day 22 No | 0 | 0 | | |
| Day 22 Missing | 1 | 1 | | |
| Day 29 Yes | 0 | 0 | | |
| Day 29 No | 0 | 0 | | |
| Day 29 Missing | 2 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From dosing until end of 90-day follow-up period, up to 91 days.

Adverse event reporting additional description:

Treated set (TS): This subject set includes all subjects who received any amount of study drug.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled |
|-----------------------|---|

Reporting group description:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of 250 milligrams (mg) of BI 767551 administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion.

| | |
|-----------------------|--|
| Reporting group title | Placebo intravenous (i.v.) + placebo inhaled |
|-----------------------|--|

Reporting group description:

Single dose of sterile normal saline (NaCl 0.9%) used as placebo was administered as intravenous (i.v.) infusion over a period of 60 minutes plus a single inhaled of solvent for dilution of BI 767551 used as placebo for inhalation administered via inhalation through a mouthpiece (Aerogen® Ultra) using a mesh nebulizer (Aerogen® Solo) on Day 1, followed by a 90-day follow-up period. The inhalation procedure was to start approximately 25 min after the start of infusion.

| Serious adverse events | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled | Placebo intravenous (i.v.) + placebo inhaled | |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

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

| Non-serious adverse events | Placebo intravenous (i.v.) + BI 767551 250 mg inhaled | Placebo intravenous (i.v.) + placebo inhaled | |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 2 / 2 (100.00%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|--|----------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 2 (50.00%) 1 | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 2 (50.00%) 1 | |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 2 (50.00%) 1 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 1 / 1 (100.00%) 1 | 1 / 2 (50.00%) 1 | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 2 (50.00%) 1 | |
| Infections and infestations Parotitis subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 2 (50.00%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 20 April 2021 | For Phase II, the number of planned patients in each treatment arm was increased from 40:40:40:20 to 50:50:50:50, and the randomisation ratio was changed from 2:2:2:1 to 1:1:1:2, in order to include more patients in the placebo intravenous (i.v.) + BI 767551 250 milligrams (mg) inhaled arm and reach an equal number of patients in each arm at the end of recruitment in Phase II. For Phase III, a treatment arm for inhaled trial drug was added as an option. |

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.

This trial was prematurely discontinued due to sponsor decision. No patients were entered in the planned Phase II "BI 10 mg/kg intravenous (i.v.) + placebo inhaled" and "BI 40 mg/kg i.v. + placebo inhaled" groups. Phase III part was not conducted.

Notes: