# Clinical trial results:
# Phase IIa (therapeutic exploratory), multicenter, randomized, double-blind, placebocontrolled, 2-stage, 4-arm study exploring the effect of BST204 on cancer-related cachexia in patients with gastrointestinal or non-small-cell lung cancer

## Summary

| | |
|---|---|
| EudraCT number | 2017-003271-61 |
| Trial protocol | DE |
| Global end of trial date | 13 October 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 25 June 2022 |
| First version publication date | 25 June 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | BST204C02 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GREEN CROSSWellbeing |
| Sponsor organisation address | 33F, Tower-2 108, Yeoui-daero, Yeongdeungpo-gu, Seoul, Korea, Republic of, 07335 |
| Public contact | Project Management, PSI CRO AG, +43 1205159911, Natalia.Peppi@psi-cro.com |
| Scientific contact | Project Management, PSI CRO AG, +43 1205159911, Natalia.Peppi@psi-cro.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 | 08 October 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 13 October 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Primary objective is to explore the efficacy of BST204 in cancer-related cachexia

Protection of trial subjects:

The Protocol and any amendments and the Informed Consent Form (ICF) were reviewed and approved by the Independent Ethics Committee (IEC) before the study was initiated. Any amendments to the Protocol or changes to the ICF required IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants. This study was conducted in accordance with the Protocol and consensus ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 06 August 2018 |
| 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 | Ukraine: 80 |
| Country: Number of subjects enrolled | Georgia: 16 |
| Country: Number of subjects enrolled | Germany: 7 |
| Worldwide total number of subjects | 103 |
| EEA total number of subjects | 7 |

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) | 64 |
| From 65 to 84 years | 39 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The studies were conducted at 18 centers across 3 countries, between 06 AUG 2018 (FPFV) and 13 OCT 2020 (LPLV).

### Pre-assignment

Screening details:

A total of 130 patients were screened, 109 (83.8%) of which met the eligibility criteria. All screening failures did not meet the eligibility criteria. One patient who met the eligibility criteria was not randomized, and 2 patients who did not meet the eligibility criteria were randomized in error. Therefore, 110 patients were randomized.

### Period 1

| | |
|---|---|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Monitor, Subject |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description: -

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

400mg (2x100mg capsules twice daily)

| | |
|---|---|
| **Arm title** | BST204 |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BST204 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

400mg (2x100mg capsules twice daily)

| **Number of subjects in period 1** | Placebo | BST204 |
|---|---|---|
| Started | 37 | 66 |
| Completed | 26 | 53 |
| Not completed | 11 | 13 |
| Consent withdrawn by subject | - | 3 |
| wrong primary endpoint test measurement | 1 | - |
| due to progress of disease | 5 | 2 |
| due to COVID-19 | - | 3 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | 4 | 3 |
| Protocol deviation | - | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | BST204 |
| Reporting group description: - | |

| Reporting group values | Placebo | BST204 | Total |
|---|---|---|---|
| Number of subjects | 37 | 66 | 103 |
| Age categorical<br>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 years and over) | 37 | 66 | 103 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 58.1 | 61.5 | |
| standard deviation | ± 11.91 | ± 8.48 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 12 | 28 | 40 |
| Male | 25 | 38 | 63 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Placebo |
| Subject analysis set type | Per protocol |

Subject analysis set description:

All patients of the Original FAS who were compliant with the exposure to the treatment regimen (at least 80% of total dose), who had no major protocol deviations, and for whom stair climb power change from baseline could be determined after 4, 8, and 12 weeks of treatment were to be included in the Original PPS.
The primary endpoint variable analysis from the Original PPS was to be used to evaluate efficacy of BST204.

| | |
|---|---|
| Subject analysis set title | BST204 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

All subjects of FAS who are compliant with the exposure to the treatment regimen (at least 80% of total dose), who have no major protocol deviations, and for whom stair climb power change from baseline can be determined after 4, 8, and 12 weeks of treatment will be included in the PPS.

| **Reporting group values** | Placebo | BST204 | |
|---|---|---|---|
| Number of subjects | 26 | 53 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18 years and over) | 26 | 53 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 55.9 | 61.6 | |
| standard deviation | ± 13.09 | ± 8.05 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 10 | 24 | |
| Male | 16 | 29 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | BST204 |
| Reporting group description: - | |
| Subject analysis set title | Placebo |
| Subject analysis set type | Per protocol |

Subject analysis set description:

All patients of the Original FAS who were compliant with the exposure to the treatment regimen (at least 80% of total dose), who had no major protocol deviations, and for whom stair climb power change from baseline could be determined after 4, 8, and 12 weeks of treatment were to be included in the Original PPS.
The primary endpoint variable analysis from the Original PPS was to be used to evaluate efficacy of BST204.

| | |
|---|---|
| Subject analysis set title | BST204 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

All subjects of FAS who are compliant with the exposure to the treatment regimen (at least 80% of total dose), who have no major protocol deviations, and for whom stair climb power change from baseline can be determined after 4, 8, and 12 weeks of treatment will be included in the PPS.

### Primary: Stair climb power test

| | |
|---|---|
| End point title | Stair climb power test |

End point description:

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

End point timeframe:

changes from baseline after 8 and 12 weeks of treatment to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: watt | | | | |
| least squares mean (standard error) | 15.59 (± 5.83) | 14.62 (± 4.08) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Efficacy |

Statistical analysis description:

The slope of stair climb power changes from baseline to week 12 of treatment with BST204 or placebo will be compared separately for each cancer group. A Mixed-effects Model Repeat Measurement (MMRM) model with baseline value as a covariate and treatment as fixed effect will be applied. For comparison of the treatments, two-sided 95% confidence intervals for the mean differences in slope and corresponding time point estimators adjusted for baseline will be computed.

| | |
|---|---|
| Comparison groups | Placebo v BST204 |
| Number of subjects included in analysis | 79 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Mixed models analysis |

## Secondary: Lean Body Mass

| | |
|---|---|
| End point title | Lean Body Mass |

End point description:

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

End point timeframe:

changes from baseline after 8 and 12 weeks of treatment to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: kg | | | | |
| least squares mean (standard error) | 0.13 (± 0.45) | -0.24 (± 0.32) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Body weight

| | |
|---|---|
| End point title | Body weight |

End point description:

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

End point timeframe:

changes from baseline after 4, 8, and 12 weeks of treatment to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: kg | | | | |
| least squares mean (standard error) | 1.48 (± 0.41) | 0.62 (± 0.29) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 6-min walking test

| End point title | 6-min walking test |
|---|---|

End point description:

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

End point timeframe:

changes from baseline after 4, 8, and 12 weeks of treatment to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: meter | | | | |
| least squares mean (standard error) | 26.36 (± 10.67) | 14.13 (± 7.47) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Handgrip strength

| End point title | Handgrip strength |
|---|---|

End point description:

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

End point timeframe:

changes from baseline after 4, 8, and 12 weeks of treatment to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: kg | | | | |
| least squares mean (standard error) | -0.04 (± 0.72) | -0.04 (± 0.50) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Quality of life (QoL)

| End point title | Quality of life (QoL) |
|---|---|

End point description:

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

End point timeframe:

changes from baseline in appetite after 4, 8, and 12 weeks of treatment in questionnaire scores (Functional Assessment of Anorexia/Cachexia [FAACT] questionnaire) to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: score | | | | |
| least squares mean (standard error) | 9.65 (± 2.43) | 2.88 (± 1.70) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Fatigue

| End point title | Fatigue |
|---|---|

End point description:

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

End point timeframe:

changes from baseline after 4, 8, and 12 weeks of treatment in questionnaire scores (Functional Assessment of Chronic Illness Therapy [FACIT] questionnaire) to obtain the slope of change from baseline to Week 12.

| End point values | Placebo | BST204 | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 26 | 53 | | |
| Units: score | | | | |
| least squares mean (standard error) | 5.69 (± 1.80) | 3.44 (± 1.26) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from baseline up to 12 weeks (End of trial) post dose, up to 2 weeks after end of trial.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | BST204 |

Reporting group description: -

| Serious adverse events | Placebo | BST204 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 37 (18.92%) | 7 / 66 (10.61%) | |
| number of deaths (all causes) | 5 | 3 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decrease | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 5 / 66 (7.58%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 66 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypochromatic anaemia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 66 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 66 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Dysphagia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 66 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 66 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoventilation | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 66 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Ureteric obstruction | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelocaliectasis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 66 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo | BST204 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 37 (83.78%) | 54 / 66 (81.82%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 7 / 66 (10.61%) | |
| occurrences (all) | 1 | 8 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 17 / 66 (25.76%) | |
| occurrences (all) | 9 | 26 | |
| Neutropenia | | | |
| subjects affected / exposed | 5 / 37 (13.51%) | 14 / 66 (21.21%) | |
| occurrences (all) | 6 | 17 | |
| Leukopenia | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 10 / 66 (15.15%) | |
| occurrences (all) | 4 | 11 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 7 / 37 (18.92%) | 8 / 66 (12.12%) | |
| occurrences (all) | 9 | 15 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 8 / 37 (21.62%) | 14 / 66 (21.21%) | |
| occurrences (all) | 10 | 25 | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 37 (13.51%) | 9 / 66 (13.64%) | |
| occurrences (all) | 8 | 16 | |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 37 (2.70%)<br>1 | 7 / 66 (10.61%)<br>8 | |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | <br><br>6 / 37 (16.22%)<br>10 | <br><br>9 / 66 (13.64%)<br>10 | |
| Metabolism and nutrition disorders<br>Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 37 (2.70%)<br>1 | <br><br>7 / 66 (10.61%)<br>8 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 21 November 2017 | - Introduction of additional pregnancy test<br>- Definition of upper limit of age<br>- Exclusion criteria regarding vital signs<br>- Revision of statement for exclusion criteria<br>- Change in notation of Sponsor name<br>- Correction of Sponsor telephone number |
| 27 February 2018 | - Change of randomization numbers<br>- Introduction of time window for Follow-up visit<br>- Introduction of calculation of the Glomerular filtration rate [GFR] at Visit 3 to 6<br>- Addition of urine sample for safety laboratory in the flow chart<br>- Revision of method description of stair climb power test<br>- Removal of fasting state for safety laboratory<br>- Revision of description for the use of flags in laboratory and vital signs listings<br>- Removal of source data book for eCRF creation |
| 06 July 2018 | - Revision of inclusion criterion regarding NSCLC diagnosis and therapy<br>- Addition of exclusion criterion regarding pacemaker<br>- Inclusion of assessment of protein-losing enteropathy at Screening<br>- Revision of withdrawal criterion regarding alpha-1-antitrypsin<br>- Deletion of measurement of LBM via DXA at Visits 3 and 4<br>- Clarification of stool collection including written consent process |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported