



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			
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			
Units: years			
arithmetic mean	58.1	61.5	
standard deviation	± 11.91	± 8.48	-
Gender categorical			
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 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 Units: years			
arithmetic mean	55.9	61.6	
standard deviation	± 13.09	± 8.05	
Gender categorical 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 (\pm 0.41)	0.62 (\pm 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 (\pm 10.67)	14.13 (\pm 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 (\pm 0.72)	-0.04 (\pm 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 (\pm 2.43)	2.88 (\pm 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 (\pm 1.80)	3.44 (\pm 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 occurrences (all)	1 / 37 (2.70%) 1	7 / 66 (10.61%) 8	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 10	9 / 66 (13.64%) 10	
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	7 / 66 (10.61%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2017	<ul style="list-style-type: none">- Introduction of additional pregnancy test- Definition of upper limit of age- Exclusion criteria regarding vital signs- Revision of statement for exclusion criteria- Change in notation of Sponsor name- Correction of Sponsor telephone number
27 February 2018	<ul style="list-style-type: none">- Change of randomization numbers- Introduction of time window for Follow-up visit- Introduction of calculation of the Glomerular filtration rate [GFR] at Visit 3 to 6- Addition of urine sample for safety laboratory in the flow chart- Revision of method description of stair climb power test- Removal of fasting state for safety laboratory- Revision of description for the use of flags in laboratory and vital signs listings- Removal of source data book for eCRF creation
06 July 2018	<ul style="list-style-type: none">- Revision of inclusion criterion regarding NSCLC diagnosis and therapy- Addition of exclusion criterion regarding pacemaker- Inclusion of assessment of protein-losing enteropathy at Screening- Revision of withdrawal criterion regarding alpha-1-antitrypsin- Deletion of measurement of LBM via DXA at Visits 3 and 4- 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