Clinical trial results:
A Phase 1-2 Ascending Dose Study to Assess the Pharmacodynamics, Pharmacokinetics, and Safety of HSP-130 in Subjects With Non-Metastatic Breast Cancer Following Single Dose and Multiple-Dose Administration By Subcutaneous Injection.

Summary

EudraCT number	2015-002057-35
Trial protocol	HU ES
Global end of trial date	05 October 2017

Results information

Result version number	v1 (current)
This version publication date	06 October 2018
First version publication date	06 October 2018

Trial information

Trial identification

Sponsor protocol code	C1221002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02650193
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.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	31 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2017
Global end of trial reached?	Yes
Global end of trial date	05 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to characterize the pharmacodynamic (PD) response of absolute neutrophil count (ANC) and CD34+ count to PF-06881894 at doses of 3 mg and 6 mg when administered as a single subcutaneous (SC) dose without chemotherapy to determine whether it would be appropriate to study multiple doses of 3 mg in the context of background chemotherapy and to characterize the PD response of duration of severe neutropenia (DSN) in Cycle 1 to PF-06881894 over a range of doses when administered as single and multiple SC doses.

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 Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2015
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	Hungary: 19
Country: Number of subjects enrolled	Spain: 6
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	17

From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of twenty-five subjects were enrolled at 3 centers in Hungary and 4 centers in Spain. Study started on 21 Dec 2015 and completed on 05 Oct 2017.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cycle 0: HSP-130 3mg

Arm description:

Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 3 milligram (mg) of HSP-130 subcutaneously (SC) at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.

Arm type	Experimental
Investigational medicinal product name	HSP-130
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 3 mg of HSP-130 SC at Day 1 of Cycle 0.

Arm title	Cycle 0: HSP-130 6mg

Arm description:

Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 6 mg of HSP-130 SC at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.

Arm type	Experimental
Investigational medicinal product name	HSP-130
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 6 mg of HSP-130 SC at Day 1 of Cycle 0.

Arm title	Cycles 1-4: HSP-130 6mg

Arm description:

Subjects in Cycles 1-4 received background chemotherapy treatment at Day 1 and were administered a single dose of 6 mg of HSP-130 SC at Day 2 of Cycles 1-4 (each cycle was approximately 3 weeks if there were no chemotherapy treatment delays). Subjects were followed approximately 30 days after last dose of study treatment.

Arm type	Experimental

Investigational medicinal product name	HSP-130
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 6 mg of HSP-130 SC at Day 2 of Cycles 1-4.

Number of subjects in period 1	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg
Started	6	6	13
Completed	6	6	13

Baseline characteristics

Reporting groups	
Reporting group title	Cycle 0: HSP-130 3mg
Reporting group description:	
Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 3 milligram (mg) of HSP-130 subcutaneously (SC) at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.	
Reporting group title	Cycle 0: HSP-130 6mg
Reporting group description:	
Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 6 mg of HSP-130 SC at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.	
Reporting group title	Cycles 1-4: HSP-130 6mg
Reporting group description:	
Subjects in Cycles 1-4 received background chemotherapy treatment at Day 1 and were administered a single dose of 6 mg of HSP-130 SC at Day 2 of Cycles 1-4 (each cycle was approximately 3 weeks if there were no chemotherapy treatment delays). Subjects were followed approximately 30 days after last dose of study treatment.	

Reporting group values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg
Number of subjects	6	6	13
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 (18-64 years)	3	3	11
From 65-84 years	3	3	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	66.8	60.8	55.1
standard deviation	± 8.89	± 13.60	± 8.95
Sex: Female, Male Units: Subjects			
Female	6	6	13
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	6	13
More than one race	0	0	0

Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	5	10
Unknown or Not Reported	0	1	3

Reporting group values	Total		
Number of subjects	25		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	17		
From 65-84 years	8		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	25		
Male	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	1		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	24		
More than one race	0		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	21		
Unknown or Not Reported	4		

End points

End points reporting groups

Reporting group title	Cycle 0: HSP-130 3mg

Reporting group description:

Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 3 milligram (mg) of HSP-130 subcutaneously (SC) at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.

Reporting group title	Cycle 0: HSP-130 6mg

Reporting group description:

Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 6 mg of HSP-130 SC at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.

Reporting group title	Cycles 1-4: HSP-130 6mg

Reporting group description:

Subjects in Cycles 1-4 received background chemotherapy treatment at Day 1 and were administered a single dose of 6 mg of HSP-130 SC at Day 2 of Cycles 1-4 (each cycle was approximately 3 weeks if there were no chemotherapy treatment delays). Subjects were followed approximately 30 days after last dose of study treatment.

Subject analysis set title	Cycle 1: HSP-130 6mg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in Cycle 1 received background chemotherapy treatment at Day 1 and were administered a single dose of 6 mg of HSP-130 SC at Day 2 of Cycle 1 (each cycle was approximately 3 weeks if there were no chemotherapy treatment delays). Subjects were followed approximately 30 days after last dose of study treatment.

Subject analysis set title	Cycle 4: HSP-130 6mg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in Cycle 4 received background chemotherapy treatment at Day 1 and were administered a single dose of 6 mg of HSP-130 SC at Day 2 of Cycle 4 (each cycle was approximately 3 weeks if there were no chemotherapy treatment delays). Subjects were followed approximately 30 days after last dose of study treatment.

Primary: Area Under the Effect Curve for Absolute Neutrophil Count (AUECANC): Cycle 0

End point title	Area Under the Effect Curve for Absolute Neutrophil Count (AUECANC): Cycle 0[1][2]

End point description:

Absolute neutrophil count (ANC) is a measure of the number of neutrophil granulocytes (also known as polymorphonuclear cells, PMN's, polys, granulocytes, segmented neutrophils or segs) present in the blood. Full Analysis Set (FAS) included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycles 1-4: HSP-130 6mg arm.

End point type	Primary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

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: Only descriptive data was planned to be analyzed for this endpoint

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour*10^9 Neutrophils per Liter				
arithmetic mean (standard deviation)	3900.482 (± 683.6870)	5880.985 (± 1287.2887)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 0

End point title	Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 0[3][4]

End point description:

AUCinf = Area under the serum concentration of HSP-130 versus time curve (AUC) from the time of dose administration to extrapolated infinite time (0-inf). FAS included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

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: Only descriptive data was planned to be analyzed for this endpoint

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour*picogram per milliliter (h*pg/mL)				
arithmetic mean (standard deviation)	1425862.2 (± 949518.8)	5689476.1 (± 3757035.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Serum Concentration (Cmax): Cycle 0

End point title	Maximum Observed Serum Concentration (Cmax): Cycle 0[5][6]

End point description:

FAS included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[5] - 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: Only descriptive data was planned to be analyzed for this endpoint

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: picogram per milliliter (pg/mL)				
arithmetic mean (standard deviation)	38026.7 (± 28821.7)	155766.7 (± 99051.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Severe Neutropenia (DSN): Cycle 1

End point title	Duration of Severe Neutropenia (DSN): Cycle 1[7]

End point description:

Severe Neutropenia was defined as grade 4 neutropenia in which the ANC was < 0.5 x10^9 per liter. DSN is defined as the days with grade 4 neutropenia (ANC < 0.5 x10^9/L). FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms. Here, ' Overall number of subjects analyzed' signifies number of subjects evaluable for the specified endpoint.

End point type	Primary

End point timeframe:

Cycle 1: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[7] - 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: Only descriptive data was planned to be analyzed for this endpoint

End point values	Cycle 1: HSP-130 6mg			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: days				
arithmetic mean (standard deviation)	0.667 (± 0.9847)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time of Last Measurable Concentration (AUCt): Cycle 1 and Cycle 4

End point title	Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time of Last Measurable Concentration (AUCt): Cycle 1 and Cycle 4[8]

End point description:

AUC0-t= Area under the serum concentration of HSP-130 versus time curve from the time of dose administration to time of last quantifiable concentration (0-t). FAS included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[8] - 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: Only descriptive data was planned to be analyzed for this endpoint

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: h*pg/mL				
arithmetic mean (standard deviation)	10084193.7 (± 14047222.7)	6017621.6 (± 5920395.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Serum Concentration (Cmax): Cycle 1 and Cycle 4

End point title	Maximum Observed Serum Concentration (Cmax): Cycle 1 and Cycle 4[9]

End point description:

FAS included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[9] - 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: Only descriptive data was planned to be analyzed for this endpoint

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: pg/mL				
arithmetic mean (standard deviation)	118130.8 (± 119028.6)	95200.0 (± 93544.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Effect for Absolute Neutrophil Count (ANC_Emax): Cycle 0

End point title	Maximum Effect for Absolute Neutrophil Count (ANC_Emax): Cycle 0[10]

End point description:

ANC is a measure of the number of neutrophil granulocytes (also known as polymorphonuclear cells, PMN's, polys, granulocytes, segmented neutrophils or segs) present in the blood. FAS included all subjects who received at least 1 dose of study medication. This end point was not planned to be analyzed for Cycles 1-4: HSP-130 6mg arm.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: *10^9 Neutrophils per Liter				
arithmetic mean (standard deviation)	24.512 (± 6.0710)	43.257 (± 5.5683)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Effect for Absolute Neutrophil Count (ANC_Tmax): Cycle 0

End point title	Time of Maximum Effect for Absolute Neutrophil Count (ANC_Tmax): Cycle 0[11]

End point description:

ANC was a measure of the number of neutrophil granulocytes (also known as polymorphonuclear cells, PMN's, polys, granulocytes, segmented neutrophils or segs) present in the blood. FAS included all subjects who received at least 1 dose of study medication. This end point was not planned to be analyzed for Cycles 1-4: HSP-130 6mg arm.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
median (full range (min-max))	71.950 (48.00 to 144.10)	47.800 (46.90 to 48.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Effect Curve for CD34+ (AUECCD34+): Cycle 0

End point title	Area Under the Effect Curve for CD34+ (AUECCD34+): Cycle

End point description:

FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycles 1-4: HSP-130 6mg arm.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour*cells per microliter (h*cells/mcL)				
arithmetic mean (standard deviation)	1749.523 (± 1022.3037)	2752.198 (± 2152.8794)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Effect for CD34+ Count (CD34+_Emax): Cycle 0

End point title	Maximum Effect for CD34+ Count (CD34+_Emax): Cycle 0[13]

End point description:

FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycles 1-4: HSP-130 6mg arm.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: cells per microliter (cells/mcL)				
arithmetic mean (standard deviation)	13.970 (± 6.8536)	27.343 (± 18.4805)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Effect for CD34+ Count (CD34+ Tmax): Cycle 0

End point title	Time of Maximum Effect for CD34+ Count (CD34+ Tmax): Cycle 0[14]

End point description:

FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycles 1-4: HSP-130 6mg arm.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
median (full range (min-max))	96.000 (48.00 to 96.10)	96.600 (95.80 to 191.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Effect Curve for Absolute Neutrophil Count From Time of Dose Administration to Time Infinity (AUEC_ANC inf): Cycle 0

End point title	Area Under the Effect Curve for Absolute Neutrophil Count From Time of Dose Administration to Time Infinity (AUEC_ANC inf): Cycle 0[15]

End point description:

ANC is a measure of the number of neutrophil granulocytes (also known as polymorphonuclear cells, PMN's, polys, granulocytes, segmented neutrophils or segs) present in the blood. FAS included all subjects who received at least 1 dose of study medication. Here, 'number of subjects analyzed' signifies number of subjects evaluable for the specified endpoint.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: hour*10^9 Neutrophils per Liter				
arithmetic mean (standard deviation)	5254.288 (± 1699.7088)	6576.165 (± 1821.9919)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Effect Curve From Time of Dose Administration to Time Infinity for CD34 + (AUEC_CD34+ inf): Cycle 0

End point title	Area Under the Effect Curve From Time of Dose Administration to Time Infinity for CD34 + (AUEC_CD34+ inf): Cycle 0[16]

End point description:

FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycles 1-4: HSP-130 6mg arm. Here, 'Overall number of subjects analyzed" signifies number of subjects evaluable for the specified endpoint.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: hour*cells per microliter (h*cells/mcL)				
arithmetic mean (standard deviation)	1835.221 (± 1036.6473)	3159.470 (± 2197.4774)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration Time Curve From the Time of Dose Administration to the Time of Last Measurable Concentration (AUCt): Cycle 0

End point title	Area Under the Serum Concentration Time Curve From the Time of Dose Administration to the Time of Last Measurable Concentration (AUCt): Cycle 0[17]

End point description:

AUC0-t= Area under the serum concentration of HSP-130 versus time curve from the time of dose administration to time of last quantifiable concentration (0-t). FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h*pg/mL				
arithmetic mean (standard deviation)	1410202.6 (± 948443.5)	5677700.3 (± 3756049.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Achieve Maximum Serum Concentration (Tmax): Cycle 0

End point title	Time To Achieve Maximum Serum Concentration (Tmax): Cycle 0[18]

End point description:

FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
median (full range (min-max))	12.0 (12 to 12)	23.5 (6 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-Life (t1/2): Cycle 0

End point title	Elimination Half-Life (t1/2): Cycle 0[19]

End point description:

t1/2 is the time taken for plasma concentration of HSP 130 to reduce by 50 percent (%) of its initial value. FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
arithmetic mean (standard deviation)	50.0 (± 15.5)	48.8 (± 12.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Rate Constant (λz): Cycle 0

End point title	Elimination Rate Constant (λz): Cycle 0[20]

End point description:

Elimination rate constant was defined as the rate at which the drug was removed from the body. FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: per hour				
arithmetic mean (standard deviation)	0.015 (± 0.0051)	0.015 (± 0.0041)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F): Cycle 0

End point title	Apparent Clearance (CL/F): Cycle 0[21]

End point description:

Clearance of a drug was defined as the rate at which a drug was metabolized or eliminated by normal biological processes. FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: milliliter per hour (mL/h)				
arithmetic mean (standard deviation)	4235.6 (± 4714.4)	1655.9 (± 1242.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 0

End point title	Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 0[22]

End point description:

The protein-content correction was conducted for AUCinf parameter: Protein-content corrected AUCinf = Nominal Protein-content AUCinf / (Actual protein concentration/10.0 mg/mL). FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h*pg/mL				
arithmetic mean (standard deviation)	1440264.8 (± 959109.9)	5689476.1 (± 3757035.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time of Last Measurable Concentration (AUCt): Cycle 0

End point title	Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time of Last Measurable Concentration (AUCt): Cycle 0[23]

End point description:

The protein-content correction was conducted for AUCt parameter: Protein-content corrected AUCt= Nominal Protein-content AUCt / (Actual protein concentration/10.0 mg/mL). FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h*pg/mL				
arithmetic mean (standard deviation)	1424447.1 (± 958023.7)	5677700.3 (± 3756049.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Protein-Content Corrected Maximum Observed Serum Concentration (Cmax): Cycle 0

End point title	Protein-Content Corrected Maximum Observed Serum Concentration (Cmax): Cycle 0[24]

End point description:

The protein-content correction was conducted for Cmax parameter: Protein-content corrected Cmax = Nominal Protein-content Cmax / (Actual protein concentration/10.0 mg/mL). FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 0: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only planned to be analyzed for the arms in the Cycle(s) identified

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: pg/mL				
arithmetic mean (standard deviation)	38410.8 (± 29112.8)	155766.7 (± 99051.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Severe Neutropenia (DSN): Cycle 4

End point title	Duration of Severe Neutropenia (DSN): Cycle 4

End point description:

Severe Neutropenia was defined as grade 4 neutropenia in which the ANC was < 0.5 x10^9/L. DSN was defined as the days with grade 4 neutropenia (ANC < 0.5 x10^9/L). FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms. Here, "Number of subjects analyzed (N)" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 4: HSP-130 6mg			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: days				
arithmetic mean (standard deviation)	0.667 (± 0.9847)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Neutrophil Count Nadir Concentration: Cycle 1 and Cycle 4

End point title	Absolute Neutrophil Count Nadir Concentration: Cycle 1 and Cycle 4

End point description:

Nadir was defined as the lowest count for ANC concentration reported after first dose of study treatment. FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: *10^9 Neutrophils per Liter				
arithmetic mean (standard deviation)	1.132 (± 1.1480)	1.623 (± 1.8364)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time of ANC Nadir Concentration: Cycle 1 and Cycle 4

End point title	Time of ANC Nadir Concentration: Cycle 1 and Cycle 4

End point description:

Time of ANC Nadir (in hours) was defined as the time from first dose of study treatment on Day 2 of Cycle 1 and 4 to the time the lowest value was recorded. FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: hour				
arithmetic mean (standard deviation)	129.231 (± 23.0585)	142.154 (± 65.3323)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Effect Curve (AUEC_ANCt): Cycle 1 and Cycle 4

End point title	Area Under the Effect Curve (AUEC_ANCt): Cycle 1 and Cycle 4

End point description:

ANC is a measure of the number of neutrophil granulocytes (also known as polymorphonuclear cells, PMN's, polys, granulocytes, segmented neutrophils or segs) present in the blood. FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: hour*10^9 Neutrophils per Liter				
arithmetic mean (standard deviation)	2540.285 (± 854.2237)	3186.542 (± 1362.0079)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Effect Curve for Absolute Neutrophil Count From Time of Dose Administration to Time Infinity (AUEC_ANC inf): Cycle 1 and Cycle 4

End point title	Area Under the Effect Curve for Absolute Neutrophil Count From Time of Dose Administration to Time Infinity (AUEC_ANC inf): Cycle 1 and Cycle 4

End point description:

Absolute neutrophil count (ANC) is a measure of the number of neutrophil granulocytes (also known as polymorphonuclear cells, PMN's, polys, granulocytes, segmented neutrophils or segs) present in the blood. FAS included all subjects who received at least 1 dose of study medication. Here, "Number of subjects analyzed (N)" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	7		
Units: hour*10^9 Neutrophils per Liter				
arithmetic mean (standard deviation)	5636.963 (± 1974.1635)	12399.370 (± 18345.3366)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Febrile Neutropenia: Cycle 1 and Cycle 4

End point title	Incidence of Febrile Neutropenia: Cycle 1 and Cycle 4

End point description:

Febrile Neutropenia was defined as tympanic or axillary body temperature greater than (>) 38.5 °C for >1 hour and ANC less than (<) 1.0 *10^9/L. FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Severe Neutropenia: Cycle 1 and Cycle 4

End point title	Incidence of Severe Neutropenia: Cycle 1 and Cycle 4

End point description:

Severe Neutropenia was defined as grade 4 neutropenia in which the ANC was < 0.5 x10^9/L. FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: subjects	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to ANC Recovery: Cycle 1 and Cycle 4

End point title	Time to ANC Recovery: Cycle 1 and Cycle 4

End point description:

Time to ANC recovery was defined as the time from documentation of the first day with ANC greater than equal to (>=) 2.0 x10^9/L after any day with ANC <2.0 x10^9/L. FAS included all subjects who received at least 1 dose of study medication. This endpoint was not planned to be analysed for Cycle 0: HSP-130 3mg and Cycle 0: HSP-130 6mg arms.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: days				
arithmetic mean (standard deviation)	2.615 (± 1.7097)	2.000 (± 1.633)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 1 and Cycle 4

End point title	Area Under the Serum Concentration Time Curve From Time of

	Dose Administration to Time Infinity (AUCinf): Cycle 1 and Cycle 4

End point description:

AUC0-inf = Area under the serum concentration versus time curve (AUC) from the time of dose administration to extrapolated infinite time (0-inf). FAS included all subjects who received at least 1 dose of study medication. Here, "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: h*pg/mL				
arithmetic mean (standard deviation)	10093213.5 (± 14047936.2)	6425013.3 (± 6000938.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Achieve Maximum Serum Concentration (Tmax): Cycle 1 and Cycle 4

End point title	Time To Achieve Maximum Serum Concentration (Tmax): Cycle 1 and Cycle 4

End point description:

FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: hour				
median (full range (min-max))	24.1 (12 to 48)	23.5 (6 to 142)		

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-Life (t1/2): Cycle 1 and Cycle 4

End point title	Elimination Half-Life (t1/2): Cycle 1 and Cycle 4

End point description:

t1/2 is the time taken for plasma concentration of a drug to reduce by 50% of its initial value. FAS included all subjects who received at least 1 dose of study medication. Here, "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: hour				
arithmetic mean (standard deviation)	30.7 (± 10.8)	29.5 (± 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Rate Constant (λz): Cycle 1 and Cycle 4

End point title	Elimination Rate Constant (λz): Cycle 1 and Cycle 4

End point description:

Elimination rate constant was defined as the rate at which the drug was removed from the body. FAS included all subjects who received at least 1 dose of study medication. Here, "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: per hour				
arithmetic mean (standard deviation)	0.026 (± 0.0099)	0.025 (± 0.0060)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F): Cycle 1 and Cycle 4

End point title	Apparent Clearance (CL/F): Cycle 1 and Cycle 4

End point description:

CL/F was defined as a quantitative measure of the rate at which a drug substance is removed from the body. FAS included all subjects who received at least 1 dose of study medication. Here, "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: mL/h				
arithmetic mean (standard deviation)	1326.8 (± 1010.2)	2342.8 (± 2043.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time of Last Measurable Concentration (AUCt): Cycle 1 and Cycle 4

End point title	Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time of Last Measurable Concentration (AUCt): Cycle 1 and Cycle 4

End point description:

The protein-content correction was conducted for AUCt parameter: Protein-content corrected AUCt= Nominal Protein-content AUCt / (Actual protein concentration/10.0 mg/mL). FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: h*pg/mL				
arithmetic mean (standard deviation)	10087666.8 (± 14045724.4)	6045733.4 (± 5955438.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 1 and Cycle 4

End point title	Protein-Content Corrected Area Under the Serum Concentration Time Curve From Time of Dose Administration to Time Infinity (AUCinf): Cycle 1 and Cycle 4

End point description:

The protein-content correction was conducted for AUCinf parameter: Protein-content corrected AUCinf = Nominal Protein-content AUCinf / (Actual protein concentration/10.0 mg/mL). FAS included all subjects who received at least 1 dose of study medication. Here, "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: h*pg/mL				
arithmetic mean (standard deviation)	10096698.3 (± 14046434.6)	6454443.8 (± 6037499.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Protein-Content Corrected Maximum Observed Serum Concentration (Cmax): Cycle 1 and Cycle 4

End point title	Protein-Content Corrected Maximum Observed Serum Concentration (Cmax): Cycle 1 and Cycle 4

End point description:

The protein-content correction was conducted for Cmax parameter: Protein-content corrected Cmax = Nominal Protein-content Cmax / (Actual protein concentration/10.0 mg/mL). FAS included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Cycle 1 and 4: Predose (0 hour), 6, 12, 24, 48, 96, 144, 192, 240 and 312 hours post-dose

End point values	Cycle 1: HSP-130 6mg	Cycle 4: HSP-130 6mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: pg/mL				
arithmetic mean (standard deviation)	118173.0 (± 119004.2)	95670.1 (± 94209.4)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence in subjects who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment Emergent Adverse Event (TEAE) was adverse event that started or worsened in severity after the HSP-130 administration up to and including 30 days post HSP-130 administration (up to Day 94). AEs included both serious and non-serious. Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects				
AEs	6	6	13	
SAEs	0	0	2	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Treatment-Emergent Adverse Events (AEs) of Special Interest

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) of Special Interest

End point description:

AEs of Special Interest (AESI) included Potential Allergic Reactions, Splenomegaly, Splenic Rupture, Acute Respiratory Distress Syndrome, Alveolar Hemorrhage, Hemoptysis, Leukocytosis,

Thrombocytopenia, Capillary Leak Syndrome, Cytokine Release Syndrome, Cutaneous Vasculitis and Glomerulonephritis. Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	0	2	2	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities

End point description:

Criteria: hematology (hemoglobin, hematocrit, platelet count, white blood cell count, neutrophils); chemistry (alkaline phosphatase, glucose, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, albumin, creatinine and gamma-glutamyl transpeptidase, blood urea nitrogen, total protein, phosphate, and uric acid); urinalysis. The clinical laboratory results and patterns observed were consistent with the known therapeutic response and the safety profile for the US and EU approved pegylated filgrastim (Neulasta).

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	6	6	13	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Clinically Significant Vital Sign Abnormalities

End point title	Number of Subjects With Clinically Significant Vital Sign Abnormalities

End point description:

Vital sign assessment included body temperature (tympanic or axillary), heart rate (sitting), blood pressure (sitting systolic and diastolic), and respiratory rate. Clinically significant abnormality was based upon investigator's discretion. Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Clinically Significant Physical Examination Abnormalities

End point title	Number of Subjects With Clinically Significant Physical Examination Abnormalities

End point description:

Physical examination included physical assessment of the spleen. Clinically significant abnormality was based on investigator’s discretion. Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Clinically Significant Electrocardiogram (ECG) Abnormalities

End point title	Number of Subjects With Clinically Significant

	Electrocardiogram (ECG) Abnormalities

End point description:

Clinically significant abnormality was based upon investigator's discretion. Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With At Least 1 Concomitant Medication

End point title	Number of Subjects With At Least 1 Concomitant Medication

End point description:

Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	6	6	13	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Duration of Exposure to Study Drug Medication

End point title	Duration of Exposure to Study Drug Medication

End point description:

Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: days				
median (full range (min-max))	3.00 (3.00 to 3.00)	6.00 (6.00 to 6.00)	24.0 (24.0 to 24.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Positive Anti-pegfilgrastim (Anti-drug) Antibodies

End point title	Number of Subjects With Positive Anti-pegfilgrastim (Anti-drug) Antibodies

End point description:

Safety analysis set included all subjects who received at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline up to approximately Day 94

End point values	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	13	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately Day 94

Adverse event reporting additional description:

Same event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Cycle 0: HSP-130 3mg

Reporting group description:

Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 3 mg of HSP-130 SC at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.

Reporting group title	Cycle 0: HSP-130 6mg

Reporting group description:

Subjects who had not received background chemotherapy treatment in the study were administered a single dose of 6 mg of HSP-130 SC at Day 1 of Cycle 0. Subjects were followed approximately 30 days after last dose of study treatment.

Reporting group title	Cycles 1-4: HSP-130 6mg

Reporting group description:

Subjects in Cycles 1-4 received background chemotherapy treatment at Day 1 and were administered a single dose of 6 mg of HSP-130 SC at Day 2 of Cycles 1-4 (each cycle was approximately 3 weeks if there were no chemotherapy treatment delays). Subjects were followed approximately 30 days after last dose of study treatment.

Serious adverse events	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cycle 0: HSP-130 3mg	Cycle 0: HSP-130 6mg	Cycles 1-4: HSP-130 6mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	13 / 13 (100.00%)
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Varicose vein			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	5
Chest discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	7
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0

Hepatic enzyme increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Seroma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nervous system disorders			
Arachnoid cyst			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Cerebral atrophy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 6 (16.67%)	4 / 6 (66.67%)	5 / 13 (38.46%)
occurrences (all)	1	6	6
Neuropathy peripheral			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Thrombocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	4 / 13 (30.77%)
occurrences (all)	0	0	7
Aphthous ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Diarrhoea			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	4 / 13 (30.77%)
occurrences (all)	0	1	4
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hyperchlorhydria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	7 / 13 (53.85%)
occurrences (all)	0	2	19
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	3 / 13 (23.08%)
occurrences (all)	1	0	4
Hepatobiliary disorders			
Hepatic cyst			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hepatomegaly			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	8 / 13 (61.54%)
occurrences (all)	0	0	8
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	3 / 13 (23.08%)
occurrences (all)	0	1	4
Intertrigo			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	4 / 13 (30.77%)
occurrences (all)	2	2	4
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	3 / 13 (23.08%)
occurrences (all)	1	1	4
Spinal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Viral infection			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 13 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported