Clinical trial results:
Randomized, OpEn-Label, Active-ContrOl Trial of SPI-2012 (Eflapegrastim) Versus Pegfilgrastim in the Management of Chemotherapy-Induced Neutropenia in Early-Stage BReast Cancer Patients Receiving Docetaxel and Cyclophosphamide (TC) (RECOVER)

Summary

EudraCT number	2016-003469-24
Trial protocol	HU
Global end of trial date	06 May 2019

Results information

Result version number	v1 (current)
This version publication date	06 February 2022
First version publication date	06 February 2022

Trial information

Trial identification

Sponsor protocol code	SPI-GCF-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02953340
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Spectrum Pharmaceuticals, Inc
Sponsor organisation address	Research and Development Office, 157 Technology Dr W, Irvine, California, United States, 92618
Public contact	Shanta Chawla, Spectrum Pharmaceuticals, Inc., +1 (949) 788-6700, shanta.chawla@sppirx.com
Scientific contact	Shanta Chawla, Spectrum Pharmaceuticals, Inc., +1 (949) 788-6700, shanta.chawla@sppirx.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	06 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to compare the efficacy of SPI-2012 versus pegfilgrastim in participants with early-stage breast cancer receiving docetaxel and cyclophosphamide (TC) to prevent and reduce neutropenia that is associated with cancer chemotherapy.

Protection of trial subjects:

This study was conducted in accordance with good clinical practice (GCP) and with the internal standard operating procedures (SOPs) of Spectrum Pharmaceuticals, Inc. A study-specific written informed consent was signed by each subject prior to any study-related assessments or procedures that were conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 May 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 24
Country: Number of subjects enrolled	Hungary: 47
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	India: 8
Country: Number of subjects enrolled	United States: 131
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 22
Worldwide total number of subjects	237
EEA total number of subjects	71

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)	153
From 65 to 84 years	83
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 74 sites in the United States, Canada, Hungary, Poland, India, Korea from 10 May 2017 to 06 May 2019. The study was conducted in two periods: treatment period (first dose of TC until 35 (± 5) days after last dose of treatment) and safety follow-up period (End of Treatment Visit through 12 months after last dose of study)

Pre-assignment

Screening details:

A total of 237 participants were randomized into study, 118 participants in Arm 1 (SPI-2012 and TC)and 119 participants in Arm 2 (Pegfilgrastim and TC). 235 participants were treated, out of which 181 participants completed the study. All participants who received at least one dose of drug (treatment period) entered the safety follow-up period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	(Arm 1): SPI-2012 and Cyclophosphamide (TC)

Arm description:

At each cycle for 4 cycles, participants received SPI-2012 at a fixed dose of 13.2 milligrams (mg)/0.6 millilitre (mL), [3.6 mg granulocyte colony-stimulating factor {G-CSF}] subcutaneously (SC) approximately 24-26 hours after receiving intravenous (IV) infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after last study treatment or patient discontinuation and long-term safety follow-up continued for 12 months after last dose of study treatment.

Arm type	Experimental
Investigational medicinal product name	SPI-2012
Investigational medicinal product code	
Other name	Eflapegrastim, HM10460A, Rolontis, LAPS-G-CSF
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

SPI-2012 13.2 mg administered SC once per cycle on Day 2.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75mg/m^2 IV infusion administered on Day 1 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Cytoxan
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cyclophosphamide 600 mg/m^2 IV infusion administered on Day 1 of each cycle.

Arm title	(Arm 2): Pegfilgrastim and TC

Arm description:

At each cycle for 4 cycles, participants received pegfilgrastim 6 mg (6 mg/0.6 mL GCSF) SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after last study treatment or patient discontinuation and long-term safety follow-up continued for 12 months after last dose of study treatment.

Arm type	Active comparator
Investigational medicinal product name	Pegfilgrastim
Investigational medicinal product code	
Other name	Neulasta
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegfilgrastim 6 mg administered SC once per cycle on Day 2.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75mg/m^2 IV infusion administered on Day 1 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Cytoxan
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cyclophosphamide 600 mg/m^2 IV infusion administered on Day 1 of each cycle.

Number of subjects in period 1	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC
Started	118	119
Entered Follow-up Period	118	119
Completed	96	85
Not completed	22	34
Consent withdrawn by subject	9	9
Death	-	1
Initiated Non-Protocol Therapy	5	14
Investigator Decision	3	3
Reason not specified	2	2
Lost to follow-up	3	2
Myeloid Growth Factors Treatment	-	1
Sponsor decision	-	2

Baseline characteristics

Reporting groups	
Reporting group title	(Arm 1): SPI-2012 and Cyclophosphamide (TC)
Reporting group description:	
At each cycle for 4 cycles, participants received SPI-2012 at a fixed dose of 13.2 milligrams (mg)/0.6 millilitre (mL), [3.6 mg granulocyte colony-stimulating factor {G-CSF}] subcutaneously (SC) approximately 24-26 hours after receiving intravenous (IV) infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after last study treatment or patient discontinuation and long-term safety follow-up continued for 12 months after last dose of study treatment.	
Reporting group title	(Arm 2): Pegfilgrastim and TC
Reporting group description:	
At each cycle for 4 cycles, participants received pegfilgrastim 6 mg (6 mg/0.6 mL GCSF) SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after last study treatment or patient discontinuation and long-term safety follow-up continued for 12 months after last dose of study treatment.	

Reporting group values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC	Total
Number of subjects	118	119	237
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	57.9	58.1	
standard deviation	± 11.27	± 12.67	-
Gender categorical Units: Subjects			
Female	118	119	237
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	18	15	33
Not Hispanic or Latino	100	104	204
Unknown or Not Reported	0	0	0
Race Units: Subjects			
Black or African American	11	7	18
Asian	20	16	36
American Indian or Alaska Native	1	0	1
Other	1	0	1
White or Caucasian	85	96	181

End points

End points reporting groups

Reporting group title	(Arm 1): SPI-2012 and Cyclophosphamide (TC)

Reporting group description:

At each cycle for 4 cycles, participants received SPI-2012 at a fixed dose of 13.2 milligrams (mg)/0.6 millilitre (mL), [3.6 mg granulocyte colony-stimulating factor {G-CSF}] subcutaneously (SC) approximately 24-26 hours after receiving intravenous (IV) infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after last study treatment or patient discontinuation and long-term safety follow-up continued for 12 months after last dose of study treatment.

Reporting group title	(Arm 2): Pegfilgrastim and TC

Reporting group description:

At each cycle for 4 cycles, participants received pegfilgrastim 6 mg (6 mg/0.6 mL GCSF) SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after last study treatment or patient discontinuation and long-term safety follow-up continued for 12 months after last dose of study treatment.

Subject analysis set title	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Treatment Period
Subject analysis set type	Safety analysis

Subject analysis set description:

At each cycle for 4 cycles, participants received SPI-2012 at a fixed dose of 13.2 mg / 0.6 mL, [3.6 mg G-CSF] SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after the last study treatment or patient discontinuation.

Subject analysis set title	Arm 2: Pegfilgrastim 6 mg and TC: Treatment Period
Subject analysis set type	Safety analysis

Subject analysis set description:

At each cycle for 4 cycles, participants received pegfilgrastim 6 mg (6 mg/0.6 mL GCSF) SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after the last study treatment or patient discontinuation.

Subject analysis set title	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Follow-up Period
Subject analysis set type	Safety analysis

Subject analysis set description:

In addition to the treatment period, long-term safety follow-up continued for 12 months after last study treatment.

Subject analysis set title	Arm 2: Pegfilgrastim 6 mg and TC: Follow-up Period
Subject analysis set type	Safety analysis

Subject analysis set description:

In addition to the treatment period, long-term safety follow-up continued for 12 months after last study treatment.

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

End point title	Duration of Severe Neutropenia (DSN) in Cycle 1

End point description:

DSN was defined as the number of days of severe neutropenia (absolute neutrophil count [ANC] <0.5×10^9 per liter [L]) from the first occurrence of ANC below the threshold. Intent-to-treat (ITT) population included all subjects who were randomized.

End point type	Primary

End point timeframe:

Day 1 and daily on Days 4-15 in Cycle 1 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	119		
Units: Days				
arithmetic mean (standard deviation)	0.31 (± 0.688)	0.39 (± 0.949)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	(Arm 1): SPI-2012 and Cyclophosphamide (TC) v (Arm 2): Pegfilgrastim and TC
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001 [2]
Method	t-statistics
Parameter estimate	Mean difference
Point estimate	-0.074
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.292
upper limit	0.129

Notes:

[1] - The study used non inferiority margin of 0.62 days for the above comparison. The non-inferiority of SPI-2012 to Pegfilgrastim was declared if the upper bound of 95% CI of the difference in mean DSN between the treatment arms was <0.62 days.

[2] - The p-values are based on the calculated t-statistics from the bootstrapped sample mean and standard deviation.

Secondary: Time to Absolute Neutrophil Count (ANC) Recovery in Cycle 1

End point title	Time to Absolute Neutrophil Count (ANC) Recovery in Cycle 1

End point description:

Time to ANC recovery was defined as the time from chemotherapy administration until the subject's ANC increased to ≥1.5×10^9/L after the expected nadir. For subjects with ANC value ≥1.5×10^9/L at all times, time to ANC Recovery was assigned a value of 0. ITT population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Day 1 and daily on Days 4-15 in Cycle 1 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	119		
Units: Days				
arithmetic mean (standard deviation)	3.49 (± 3.723)	3.35 (± 3.745)		

Statistical analyses

No statistical analyses for this end point

Secondary: Depth of ANC Nadir in Cycle 1

End point title	Depth of ANC Nadir in Cycle 1

End point description:

The depth of ANC Nadir was defined as the lowest ANC value after administration of study drug (SPI-2012 or pegfilgrastim) in Cycle 1. ITT population included all subjects who were randomized. Here 'N' (number of subjects analysed) signifies the number of subjects evaluable for this endpoint at the specified timepoint.

End point type	Secondary

End point timeframe:

Day 1 and daily on Days 4-15 in Cycle 1 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	116		
Units: x10^9/L				
arithmetic mean (standard deviation)	2.67 (± 3.504)	2.06 (± 2.034)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Febrile Neutropenia (FN) in Cycle 1

End point title	Number of Subjects with Febrile Neutropenia (FN) in Cycle 1

End point description:

FN was defined as an oral temperature >38.3 degree Celsius (°C) (101.0 degrees Fahrenheit [°F]) or two consecutive readings of >38.0°C (100.4°F) for 2 hours and ANC <1.0×10^9/L. ITT population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Day 1 and daily on Days 4-15 in Cycle 1 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	119		
Units: Subjects	1	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Severe Neutropenia (DSN) in Cycles 2, 3 and 4

End point title	Duration of Severe Neutropenia (DSN) in Cycles 2, 3 and 4

End point description:

DSN was defined as the number of days of severe neutropenia (ANC <0.5×10^9/L) from the first occurrence of ANC below the threshold. ITT population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Days 1, 4, 7, 10, and 15 of Cycles 2, 3, and 4 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	119		
Units: Days				
arithmetic mean (standard deviation)				
Cycle 2	0.08 (± 0.267)	0.09 (± 0.432)		
Cycle 3	0.07 (± 0.252)	0.07 (± 0.283)		
Cycle 4	0.07 (± 0.252)	0.08 (± 0.266)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Neutropenic Complications in Cycle 1

End point title	Number of Subjects with Neutropenic Complications in Cycle 1

End point description:

Neutropenic complications refer to hospitalizations due to neutropenic events and/or the use of anti-infectives due to neutropenia. ITT population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Day 1 and daily on Days 4-15 in Cycle 1 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	119		
Units: Subjects	1	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Febrile Neutropenia in Cycles 2, 3 and 4

End point title	Number of Subjects with Febrile Neutropenia in Cycles 2, 3 and 4

End point description:

FN was defined as an oral temperature >38.3°C (101.0°F) or two consecutive readings of >38.0°C (100.4°F) for 2 hours and ANC <1.0×10^9/L. ITT population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Days 1, 4, 7, 10, and 15 of Cycles 2, 3, and 4 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	119		
Units: Subjects				
Cycle 2	0	2		
Cycle 3	0	0		
Cycle 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Dose Intensity (RDI) of TC Chemotherapy

End point title	Relative Dose Intensity (RDI) of TC Chemotherapy

End point description:

RDI was defined as the percentage of the planned dose of TC chemotherapy that each participant actually received during the study, and is expressed as the total dose received, divided by total dose planned multiplied by 100. The planned dose was defined as the dose that would be given if no doses were missed and/or no dose reductions were made for the number of cycles started. The total planned dose was the sum of planned doses over all cycles. Safety analysis (SAF) population included all subjects who received at least one dose of any protocol-specified drug (TC or SPI-2012 or pegfilgrastim).

End point type	Secondary

End point timeframe:

Cycles 1, 2, 3 and 4 (each cycle = 21 days)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	118		
Units: Percentage of planned dose				
arithmetic mean (standard deviation)				
Docetaxel	96.9 (± 7.70)	98.4 (± 7.89)		
Cyclophosphamide	98.4 (± 5.27)	98.8 (± 6.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs), and Death

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs), and Death

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product or study procedure, whether or not considered related to the medicinal product. A TEAE is any AE that occurred from the first dose of study treatment through 12 months after the last dose of study treatment or 35 (±5) days after date of participant early discontinuation. SAE is defined as any AE which meets any of the following criteria: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in a persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, includes important medical events. SAF population included all subjects who received at least one dose of any protocol-specified drug (TC or SPI-2012 or pegfilgrastim). Data was summarized and reported for Treatment and Follow-up period separately for both groups.

End point type	Secondary

End point timeframe:

Up to 4 cycles (each cycle = 21 days) plus a 12-month follow-up from the last dose (up to 15 months)

End point values	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Treatment Period	Arm 2: Pegfilgrastim 6 mg and TC: Treatment Period	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Follow-up Period	Arm 2: Pegfilgrastim 6 mg and TC: Follow-up Period
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	117	118	117	118
Units: Subjects				
TEAEs	115	116	33	48
SAEs	12	19	2	4
Death	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Laboratory Abnormalities

End point title	Number of Subjects with Clinically Significant Laboratory Abnormalities

End point description:

The number of subjects with clinically significant hematology (including basophils, basophils/leukocytes, eosinophils, eosinophils/leukocytes, hematocrit, hemoglobin, lymphocytes, lymphocytes/leukocytes, monocytes, monocytes/leukocytes, neutrophils, neutrophils/leukocytes, platelets, and white blood cells) and serum chemistry (including alanine aminotransferase [ALT], alkaline phosphatase [ALP], aspartate aminotransferase [AST], bilirubin, calcium, cholesterol, creatinine, potassium, sodium, and triglycerides) laboratory abnormalities were reported. SAF population included all subjects who received at least one dose of any protocol-specified drug (TC or SPI-2012 or pegfilgrastim).

End point type	Secondary

End point timeframe:

Up to 4 cycles (each cycle = 21 days) plus a 12-month follow-up from the last dose (up to 15 months)

End point values	(Arm 1): SPI-2012 and Cyclophosphamide (TC)	(Arm 2): Pegfilgrastim and TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	118		
Units: Subjects				
Hematology: Basophils	0	0		
Hematology: Basophils/Leukocytes	0	0		
Hematology: Eosinophils	0	0		
Hematology: Eosinophils/Leukocytes	0	0		
Hematology: Hematocrit	4	2		
Hematology: Hemoglobin	6	4		
Hematology: Lymphocytes	0	0		
Hematology: Lymphocytes/Leukocytes	6	13		
Hematology: Monocytes	0	0		
Hematology: Monocytes/Leukocytes	0	0		
Hematology: Neutrophils	17	23		
Hematology: Neutrophils/Leukocytes	12	9		

Hematology: Platelets	10	2		
Hematology: White Blood Cells	16	18		
Chemistry: ALT	2	1		
Chemistry: ALP	0	1		
Chemistry: AST	1	1		
Chemistry: Bilirubin	0	0		
Chemistry: Calcium	1	1		
Chemistry: Cholesterol	0	0		
Chemistry: Creatinine	0	0		
Chemistry: Potassium	0	1		
Chemistry: Sodium	0	2		
Chemistry: Triglycerides	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 4 cycles (each cycle = 21 days) plus a 12-month follow-up from the last dose (up to 15 months)

Adverse event reporting additional description:

The Safety Analysis Population included all participants who received at least one dose of any protocol-specified drug (TC or SPI-2012 or pegfilgrastim). Adverse events data was summarized and reported for Treatment and Follow-up period separately for both groups.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Treatment Period

Reporting group description:

At each cycle for 4 cycles, participants received SPI-2012 at a fixed dose of 13.2 mg / 0.6 mL, [3.6 mg G-CSF] SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after the last study treatment or patient discontinuation.

Reporting group title	Arm 2: Pegfilgrastim 6 mg and TC: Treatment Period

Reporting group description:

At each cycle for 4 cycles, participants received pegfilgrastim 6 mg (6 mg/0.6 mL GCSF) SC approximately 24-26 hours after receiving IV infusion of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 IV infusion per institute's standard of care. All participants were followed for 35 (±5) days after the last study treatment or patient discontinuation.

Reporting group title	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Follow-up Period

Reporting group description:

In addition to the treatment period, long-term safety follow-up continued for 12 months after last study treatment.

Reporting group title	Arm 2: Pegfilgrastim 6 mg and TC: Follow-up Period

Reporting group description:

In addition to the treatment period, long-term safety follow-up continued for 12 months after last study treatment.

Serious adverse events	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Treatment Period	Arm 2: Pegfilgrastim 6 mg and TC: Treatment Period	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Follow-up Period
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 117 (10.26%)	19 / 118 (16.10%)	2 / 117 (1.71%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypotension			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Administration site reaction			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 117 (0.85%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 117 (0.85%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 117 (0.00%)	2 / 118 (1.69%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Neutrophil count decreased			

subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 117 (1.71%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac arrest			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 117 (0.00%)	2 / 118 (1.69%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 117 (0.00%)	3 / 118 (2.54%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin disorder			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 117 (0.85%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis viral			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest wall abscess			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 117 (0.00%)	2 / 118 (1.69%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 117 (0.85%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 117 (0.00%)	1 / 118 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm 2: Pegfilgrastim 6 mg and TC: Follow-up Period		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 118 (3.39%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Administration site reaction			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Neutrophil count decreased			

subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament sprain				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seroma				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Sinus tachycardia				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cardiac arrest			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin disorder				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bronchitis				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Bronchitis viral				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest wall abscess				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 118 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid overload			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Treatment Period	Arm 2: Pegfilgrastim 6 mg and TC: Treatment Period	Arm 1: SPI-2012 13.2 mg/0.6 mL and TC: Follow-up Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 117 (98.29%)	116 / 118 (98.31%)	33 / 117 (28.21%)
Vascular disorders			
Flushing			
subjects affected / exposed	9 / 117 (7.69%)	10 / 118 (8.47%)	0 / 117 (0.00%)
occurrences (all)	12	12	0
Hot flush			
subjects affected / exposed	10 / 117 (8.55%)	8 / 118 (6.78%)	1 / 117 (0.85%)
occurrences (all)	10	8	1
Hypertension			

subjects affected / exposed	4 / 117 (3.42%)	8 / 118 (6.78%)	1 / 117 (0.85%)
occurrences (all)	13	17	1
Hypotension			
subjects affected / exposed	6 / 117 (5.13%)	3 / 118 (2.54%)	0 / 117 (0.00%)
occurrences (all)	6	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	40 / 117 (34.19%)	51 / 118 (43.22%)	0 / 117 (0.00%)
occurrences (all)	59	72	0
Pyrexia			
subjects affected / exposed	25 / 117 (21.37%)	26 / 118 (22.03%)	1 / 117 (0.85%)
occurrences (all)	41	43	1
Oedema peripheral			
subjects affected / exposed	12 / 117 (10.26%)	15 / 118 (12.71%)	2 / 117 (1.71%)
occurrences (all)	18	21	3
Asthenia			
subjects affected / exposed	15 / 117 (12.82%)	11 / 118 (9.32%)	0 / 117 (0.00%)
occurrences (all)	18	16	0
Pain			
subjects affected / exposed	5 / 117 (4.27%)	11 / 118 (9.32%)	0 / 117 (0.00%)
occurrences (all)	5	12	0
Chills			
subjects affected / exposed	4 / 117 (3.42%)	6 / 118 (5.08%)	0 / 117 (0.00%)
occurrences (all)	5	9	0
Malaise			
subjects affected / exposed	3 / 117 (2.56%)	6 / 118 (5.08%)	0 / 117 (0.00%)
occurrences (all)	4	11	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	8 / 117 (6.84%)	17 / 118 (14.41%)	2 / 117 (1.71%)
occurrences (all)	12	21	3
Cough			
subjects affected / exposed	8 / 117 (6.84%)	14 / 118 (11.86%)	1 / 117 (0.85%)
occurrences (all)	9	18	2
Oropharyngeal pain			

subjects affected / exposed	9 / 117 (7.69%)	10 / 118 (8.47%)	0 / 117 (0.00%)
occurrences (all)	9	12	0
Epistaxis			
subjects affected / exposed	4 / 117 (3.42%)	7 / 118 (5.93%)	0 / 117 (0.00%)
occurrences (all)	7	9	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	18 / 117 (15.38%)	11 / 118 (9.32%)	1 / 117 (0.85%)
occurrences (all)	22	11	1
Anxiety			
subjects affected / exposed	5 / 117 (4.27%)	8 / 118 (6.78%)	0 / 117 (0.00%)
occurrences (all)	5	8	0
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	44 / 117 (37.61%)	54 / 118 (45.76%)	0 / 117 (0.00%)
occurrences (all)	69	109	0
White blood cell count decreased			
subjects affected / exposed	22 / 117 (18.80%)	31 / 118 (26.27%)	1 / 117 (0.85%)
occurrences (all)	30	59	2
Neutrophil count decreased			
subjects affected / exposed	16 / 117 (13.68%)	22 / 118 (18.64%)	1 / 117 (0.85%)
occurrences (all)	30	49	1
Platelet count decreased			
subjects affected / exposed	12 / 117 (10.26%)	3 / 118 (2.54%)	0 / 117 (0.00%)
occurrences (all)	17	4	0
White blood cell count increased			
subjects affected / exposed	9 / 117 (7.69%)	3 / 118 (2.54%)	0 / 117 (0.00%)
occurrences (all)	11	4	0
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	2 / 117 (1.71%)
occurrences (all)	1	0	2
Cardiac disorders			
Tachycardia			
subjects affected / exposed	5 / 117 (4.27%)	6 / 118 (5.08%)	0 / 117 (0.00%)
occurrences (all)	6	9	0

Nervous system disorders			
Headache			
subjects affected / exposed	31 / 117 (26.50%)	35 / 118 (29.66%)	0 / 117 (0.00%)
occurrences (all)	50	43	0
Dysgeusia			
subjects affected / exposed	9 / 117 (7.69%)	16 / 118 (13.56%)	0 / 117 (0.00%)
occurrences (all)	10	19	0
Neuropathy peripheral			
subjects affected / exposed	9 / 117 (7.69%)	14 / 118 (11.86%)	1 / 117 (0.85%)
occurrences (all)	14	16	0
Dizziness			
subjects affected / exposed	6 / 117 (5.13%)	12 / 118 (10.17%)	1 / 117 (0.85%)
occurrences (all)	7	15	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	37 / 117 (31.62%)	37 / 118 (31.36%)	0 / 117 (0.00%)
occurrences (all)	77	59	0
Anaemia			
subjects affected / exposed	22 / 117 (18.80%)	11 / 118 (9.32%)	1 / 117 (0.85%)
occurrences (all)	33	26	1
Lymphopenia			
subjects affected / exposed	10 / 117 (8.55%)	9 / 118 (7.63%)	1 / 117 (0.85%)
occurrences (all)	18	13	1
Eye disorders			
Lacrimation increased			
subjects affected / exposed	2 / 117 (1.71%)	7 / 118 (5.93%)	0 / 117 (0.00%)
occurrences (all)	3	8	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	50 / 117 (42.74%)	61 / 118 (51.69%)	1 / 117 (0.85%)
occurrences (all)	97	107	1
Diarrhoea			
subjects affected / exposed	38 / 117 (32.48%)	40 / 118 (33.90%)	1 / 117 (0.85%)
occurrences (all)	74	60	1
Constipation			
subjects affected / exposed	26 / 117 (22.22%)	24 / 118 (20.34%)	0 / 117 (0.00%)
occurrences (all)	29	31	0

Abdominal pain			
subjects affected / exposed	14 / 117 (11.97%)	20 / 118 (16.95%)	0 / 117 (0.00%)
occurrences (all)	20	22	0
Vomiting			
subjects affected / exposed	14 / 117 (11.97%)	19 / 118 (16.10%)	1 / 117 (0.85%)
occurrences (all)	15	26	1
Dyspepsia			
subjects affected / exposed	14 / 117 (11.97%)	9 / 118 (7.63%)	1 / 117 (0.85%)
occurrences (all)	14	10	1
Stomatitis			
subjects affected / exposed	9 / 117 (7.69%)	10 / 118 (8.47%)	0 / 117 (0.00%)
occurrences (all)	10	13	0
Dry mouth			
subjects affected / exposed	3 / 117 (2.56%)	9 / 118 (7.63%)	0 / 117 (0.00%)
occurrences (all)	3	9	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	40 / 117 (34.19%)	43 / 118 (36.44%)	1 / 117 (0.85%)
occurrences (all)	41	46	1
Rash			
subjects affected / exposed	13 / 117 (11.11%)	11 / 118 (9.32%)	0 / 117 (0.00%)
occurrences (all)	21	15	0
Pruritus			
subjects affected / exposed	10 / 117 (8.55%)	9 / 118 (7.63%)	0 / 117 (0.00%)
occurrences (all)	11	11	0
Erythema			
subjects affected / exposed	4 / 117 (3.42%)	6 / 118 (5.08%)	0 / 117 (0.00%)
occurrences (all)	5	7	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	47 / 117 (40.17%)	51 / 118 (43.22%)	1 / 117 (0.85%)
occurrences (all)	91	85	1
Myalgia			
subjects affected / exposed	26 / 117 (22.22%)	23 / 118 (19.49%)	0 / 117 (0.00%)
occurrences (all)	44	39	0
Back pain			

subjects affected / exposed	18 / 117 (15.38%)	15 / 118 (12.71%)	2 / 117 (1.71%)
occurrences (all)	21	15	2
Arthralgia			
subjects affected / exposed	17 / 117 (14.53%)	12 / 118 (10.17%)	4 / 117 (3.42%)
occurrences (all)	21	17	4
Pain in extremity			
subjects affected / exposed	14 / 117 (11.97%)	11 / 118 (9.32%)	1 / 117 (0.85%)
occurrences (all)	17	20	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	5 / 117 (4.27%)	9 / 118 (7.63%)	1 / 117 (0.85%)
occurrences (all)	7	9	1
Nasopharyngitis			
subjects affected / exposed	3 / 117 (2.56%)	6 / 118 (5.08%)	1 / 117 (0.85%)
occurrences (all)	3	6	1
Urinary tract infection			
subjects affected / exposed	3 / 117 (2.56%)	7 / 118 (5.93%)	0 / 117 (0.00%)
occurrences (all)	3	7	0
Candida infection			
subjects affected / exposed	1 / 117 (0.85%)	7 / 118 (5.93%)	0 / 117 (0.00%)
occurrences (all)	1	8	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	23 / 117 (19.66%)	19 / 118 (16.10%)	0 / 117 (0.00%)
occurrences (all)	26	21	0
Hypokalaemia			
subjects affected / exposed	4 / 117 (3.42%)	8 / 118 (6.78%)	2 / 117 (1.71%)
occurrences (all)	4	12	2
Dehydration			
subjects affected / exposed	3 / 117 (2.56%)	8 / 118 (6.78%)	0 / 117 (0.00%)
occurrences (all)	3	10	0

Non-serious adverse events	Arm 2: Pegfilgrastim 6 mg and TC: Follow-up Period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 118 (40.68%)		

Vascular disorders			
Flushing			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		
Hot flush			
subjects affected / exposed	3 / 118 (2.54%)		
occurrences (all)	3		
Hypertension			
subjects affected / exposed	3 / 118 (2.54%)		
occurrences (all)	4		
Hypotension			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Cough subjects affected / exposed occurrences (all)	1 / 118 (0.85%) 1		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Epistaxis subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 118 (0.85%) 1		
Anxiety subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Investigations Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 118 (0.85%) 1		
White blood cell count decreased subjects affected / exposed occurrences (all)	2 / 118 (1.69%) 2		
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
White blood cell count increased subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Injury, poisoning and procedural complications			

Radiation skin injury subjects affected / exposed occurrences (all)	6 / 118 (5.08%) 6		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	1 / 118 (0.85%) 1 0 / 118 (0.00%) 0 1 / 118 (0.85%) 1 1 / 118 (0.85%) 0		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0 2 / 118 (1.69%) 2 0 / 118 (0.00%) 0		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	1 / 118 (0.85%) 1		
Gastrointestinal disorders Nausea			

subjects affected / exposed	1 / 118 (0.85%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	3 / 118 (2.54%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	3 / 118 (2.54%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	3 / 118 (2.54%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	7 / 118 (5.93%)		
occurrences (all)	7		
Pain in extremity			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	3 / 118 (2.54%)		
occurrences (all)	4		
Candida infection			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 118 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences (all)	2		

Dehydration subjects affected / exposed occurrences (all)	0 / 118 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 July 2017	The overall reason for this amendment was to make sure that the eligibility criteria and procedures for SPI-GCF-302 matched the criteria in the other Phase 3 trial, SPI-GCF-301.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported