



Clinical trial results:

A randomized and open-label dose-finding, phase 2, efficacy, safety, and pharmacokinetic study of once-per-cycle prophylactic injections of ANF-RHO™ versus pegfilgrastim (Neulasta®) in non-metastatic breast cancer patients at high risk of chemotherapy-induced neutropenia (CIN)

Summary

EudraCT number	2016-001965-98
Trial protocol	NL
Global end of trial date	17 January 2019

Results information

Result version number	v1 (current)
This version publication date	11 February 2020
First version publication date	11 February 2020

Trial information

Trial identification

Sponsor protocol code	PGFN-001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Prolong Pharmaceuticals, LLC
Sponsor organisation address	300 Corporate Court, Suite B, South Plainfield, New Jersey, United States, 07080
Public contact	Tara Chapman, Prolong Pharmaceuticals, LLC, 1 6095571237, tchapman@prolongmail.com
Scientific contact	Tara Chapman, Prolong Pharmaceuticals, LLC, 1 6095571237, tchapman@prolongmail.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	19 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2018
Global end of trial reached?	Yes
Global end of trial date	17 January 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To assess the efficacy of escalating doses of ANF-RHO versus Neulasta in the duration of neutropenia grade 1 or worse (absolute neutrophil count [ANC] $\leq 2.0 \times 10^9/L$) in the first chemotherapy cycle (21-day cycle FE100C).

Protection of trial subjects:

The clinical study discussed in this report was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulatory requirements. The Investigator must explain to each patient (or legally authorized representative) or parent the nature of the study, the purpose, the procedures involved, the expected duration, the potential benefits and risks involved, and any discomfort it may entail. The study drug should be identified as investigational (experimental) and that its side effects are not completely known. This information must be provided in language that the patient understands. Each patient must be informed that participation in the study is voluntary and that they may withdraw from the study at any time, and that withdrawal of consent will not affect their subsequent medical treatment or relationship with the treating physician. The patient should read and consider the statement before signing and dating it and should be given a copy of the signed document. No patient can enter the study before written informed consent/ assent has been obtained. The Investigator must assure that Patients' anonymity will be strictly maintained and that their identities are protected from unauthorized parties.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2017
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	Netherlands: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	8
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from 4 sites in the Netherlands from 03 Aug 2017 through 22 May 2018.

Pre-assignment

Screening details:

Scheduled to receive and anticipated to complete the following chemotherapy regimen: FEC (flourouracil/epirubicin) [100]/cyclophosphamide (3 cycles); docetaxel (3 cycles) chemotherapy

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

10 µg/kg ANF-RHO on Cycle Day 1

Arm type	Experimental
Investigational medicinal product name	ANF-RHO
Investigational medicinal product code	PP-103
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

10 µg/kg ANF-RHO by subcutaneous injection, once per chemotherapy cycle on Day 1

Arm title	Cohort 4
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Arm description:

6 mg Neulasta on Cycle Day 2

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

Dosage and administration details:

6 mg Neulasta on Cycle Day 2

Number of subjects in period 1	Cohort 1	Cohort 4
Started	7	2
Completed	4	2
Not completed	3	0
Adverse event, non-fatal	1	-

Lack of efficacy	2	-
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Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
Reporting group description: 10 µg/kg ANF-RHO on Cycle Day 1	
Reporting group title	Cohort 4
Reporting group description: 6 mg Neulasta on Cycle Day 2	

Reporting group values	Cohort 1	Cohort 4	Total
Number of subjects	7	2	9
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)	6	2	8
From 65-84 years	1	0	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55	59.5	
full range (min-max)	36 to 69	58 to 61	-
Gender categorical Units: Subjects			
Female	7	2	9
Male	0	0	0

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: 10 µg/kg ANF-RHO on Cycle Day 1	
Reporting group title	Cohort 4
Reporting group description: 6 mg Neulasta on Cycle Day 2	

Primary: Duration of neutropenia grade 1 or worse (absolute neutrophil count [ANC] ≤ 2.0 x 10⁹/L) in the first cycle of chemotherapy (FE100C).

End point title	Duration of neutropenia grade 1 or worse (absolute neutrophil count [ANC] ≤ 2.0 x 10 ⁹ /L) in the first cycle of chemotherapy (FE100C). ^[1]
End point description:	
End point type	Primary
End point timeframe: First cycle of Chemotherapy (FE100C)	

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: Study terminated early, no statistical analysis conducted

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: Time				

Notes:

[2] - Study terminated early, no statistical analysis conducted

[3] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of neutropenia grade 1 or worse (absolute neutrophil count [ANC] ≤ 2.0 x 10⁹/L) in the fourth cycle of chemotherapy (docetaxel).

End point title	Duration of neutropenia grade 1 or worse (absolute neutrophil count [ANC] ≤ 2.0 x 10 ⁹ /L) in the fourth cycle of chemotherapy (docetaxel).
End point description:	
End point type	Secondary
End point timeframe: Fourth cycle of chemotherapy (docetaxel)	

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: Time				

Notes:

[4] - Study terminated early, no statistical analysis conducted

[5] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of severe neutropenia (ANC < 0.5 x 10⁹/L) during the first chemotherapy cycle (21-day cycle FE100C)

End point title	Duration of severe neutropenia (ANC < 0.5 x 10 ⁹ /L) during the first chemotherapy cycle (21-day cycle FE100C)
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End point description:

End point type	Secondary
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End point timeframe:

First chemotherapy cycle (21-day cycle FE100C)

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: Time				

Notes:

[6] - Study terminated early, no statistical analysis conducted

[7] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of severe neutropenia (ANC < 0.5 x 10⁹/L) during the fourth chemotherapy cycle (21-day cycle docetaxel)

End point title	Duration of severe neutropenia (ANC < 0.5 x 10 ⁹ /L) during the fourth chemotherapy cycle (21-day cycle docetaxel)
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End point description:

End point type	Secondary
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End point timeframe:

Fourth chemotherapy cycle (21-day cycle docetaxel)

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	0 ^[9]		
Units: Time				

Notes:

[8] - Study terminated early, no statistical analysis conducted

[9] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of severe neutropenia (ANC < 0.5 x 10⁹/L) during all chemotherapy cycles

End point title	Incidence of severe neutropenia (ANC < 0.5 x 10 ⁹ /L) during all chemotherapy cycles
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End point description:

End point type	Secondary
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End point timeframe:

During all chemotherapy cycles

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[10]	0 ^[11]		
Units: events of severe neutropenia				

Notes:

[10] - Study terminated early, no statistical analysis conducted

[11] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and duration of febrile neutropenia defined as peak temperature ≥38.5°C (or ≥38.0°C for two readings over two hours) and ANC < 0.5 x 10⁹/L, during all chemotherapy cycles

End point title	Incidence and duration of febrile neutropenia defined as peak temperature ≥38.5°C (or ≥38.0°C for two readings over two hours) and ANC < 0.5 x 10 ⁹ /L, during all chemotherapy cycles
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End point description:

End point type	Secondary
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End point timeframe:

during all chemotherapy cycles

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[12]	0 ^[13]		
Units: events of severe neutropenia & time				

Notes:

[12] - Study terminated early, no statistical analysis conducted

[13] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and duration of infection and infection-related events (e.g., antibiotic use, need for hospitalization, etc.) during all chemotherapy cycles

End point title	Incidence and duration of infection and infection-related events (e.g., antibiotic use, need for hospitalization, etc.) during all chemotherapy cycles
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End point description:

End point type	Secondary
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End point timeframe:

all chemotherapy cycles

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[14]	0 ^[15]		
Units: Incidence & time				

Notes:

[14] - Study terminated early, no statistical analysis conducted

[15] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and duration of moderate (ANC $\geq 50 \times 10^9/L$) and severe (ANC $\geq 100 \times 10^9/L$) leukocytosis during all chemotherapy cycles

End point title	Incidence and duration of moderate (ANC $\geq 50 \times 10^9/L$) and severe (ANC $\geq 100 \times 10^9/L$) leukocytosis during all chemotherapy cycles
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End point description:

End point type	Secondary
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End point timeframe:

during all chemotherapy cycles

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[16]	0 ^[17]		
Units: Incidence & time				

Notes:

[16] - Study terminated early, no statistical analysis conducted

[17] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically meaningful changes in vital signs during all chemotherapy cycles

End point title	Clinically meaningful changes in vital signs during all chemotherapy cycles
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End point description:

End point type	Secondary
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End point timeframe:

during all chemotherapy cycles

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[18]	0 ^[19]		
Units: vital signs				
number (not applicable)				

Notes:

[18] - Study terminated early, no statistical analysis conducted

[19] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence, duration, severity and site of bone pain, determined by a numerical rating scale, as well as other reported adverse events

End point title	Incidence, duration, severity and site of bone pain, determined by a numerical rating scale, as well as other reported adverse events
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End point description:

End point type	Secondary
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End point timeframe:

Through the completion of the clinical trial

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[20]	0 ^[21]		
Units: numerical rating scale				
number (not applicable)				

Notes:

[20] - Study terminated early, no statistical analysis conducted

[21] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of ANF-RHO and Neulasta

End point title	Pharmacokinetic profile of ANF-RHO and Neulasta
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End point description:

End point type	Secondary
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End point timeframe:

through the end of the clinical trial

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[22]	0 ^[23]		
Units: pharmacokinetic profile				
number (not applicable)				

Notes:

[22] - Study terminated early, no statistical analysis conducted

[23] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-drug antibodies to ANF-RHO and Neulasta

End point title	Incidence of anti-drug antibodies to ANF-RHO and Neulasta
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End point description:

End point type	Secondary
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End point timeframe:

Through the end of the clinical trial

End point values	Cohort 1	Cohort 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[24]	0 ^[25]		
Units: Incidence of anti-drug antibodies				

Notes:

[24] - Study terminated early, no statistical analysis conducted

[25] - Study terminated early, no statistical analysis conducted

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Continuous and 3 ± 2 days following study completion or early discontinuation; discontinuation due to study-related adverse event will be followed for 30 days or until the resolution or stabilization of the event

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

10 µg/kg ANF-RHO on Cycle Day 1

Reporting group title	Cohort 4
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Reporting group description:

6 mg Neulasta on Cycle Day 2

Serious adverse events	Cohort 1	Cohort 4	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			

subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vitreous detachment			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1	Cohort 4	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	2 / 2 (100.00%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 7 (57.14%)	2 / 2 (100.00%)	
occurrences (all)	4	4	
Mucosal inflammation			

subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2 2 / 7 (28.57%) 2	1 / 2 (50.00%) 1 1 / 2 (50.00%) 1	
Immune system disorders Allergy to chemicals subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	0 / 2 (0.00%) 0	
Reproductive system and breast disorders Vulvovaginal inflammation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1 1 / 7 (14.29%) 2 1 / 7 (14.29%) 1	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0	
Investigations Gastric pH decreased subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	0 / 2 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Polyneuropathy	2 / 7 (28.57%) 2	1 / 2 (50.00%) 1	

subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Taste disorder subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	5 / 7 (71.43%) 6	0 / 2 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 5	1 / 2 (50.00%) 1	
Vomiting subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3	0 / 2 (0.00%) 0	
Stomatitis subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Constipation			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Dry mouth subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Dyspepsia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Glossodynia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	5 / 7 (71.43%) 5	2 / 2 (100.00%) 2	
Rash subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Onychalgia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Rosacea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Skin reaction subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	0 / 2 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Bone pain subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 4	1 / 2 (50.00%) 1	
Back pain subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Musculoskeletal pain			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Infections and infestations Herpes zoster subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Oral herpes subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 2 (0.00%) 0	
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 2 (50.00%) 1	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated for business reasons because changes in standard of care were impractical to address. Limited study enrollment does not allow for efficacy analyses to be conducted.

Notes: