Clinical trial results:
A randomized, double blind, multicenter study assessing short (16 weeks) and long term efficacy (up to 1 year), safety, and tolerability of sub cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque type psoriasis

Summary

EudraCT number	2015-004620-60
Trial protocol	DE HU IT
Global end of trial date	15 July 2020

Results information

Result version number	v1 (current)
This version publication date	29 May 2021
First version publication date	29 May 2021

Trial information

Trial identification

Sponsor protocol code	CAIN457A2324

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03504852
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	15 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of secukinumab 300 mg every 2 weeks in comparison to secukinumab 300 mg every 4 weeks with respect to Psoriasis Area and Severity Index (PASI) 90 response at Week 16.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	Germany: 51
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	United States: 161
Worldwide total number of subjects	331
EEA total number of subjects	103

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	300
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

331 participants in the study were randomized and 330 participants were treated. (One participant in the AIN457 300mg Q4W (safety) arm was randomized but not treated. This participant was included in the randomization (demographic and disposition) set and the full analysis set, but was not included in the safety (Adverse Events) set.)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 300 mg every 2 weeks (Q2W)

Arm description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab 150 mg solution for subcutaneous (sc) injection in a 1 mL prefilled syringe (PFS).

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo solution for sc injection in a 1 mL PFS matching the composition and appearance of secukinumab 150 mg dose

Arm title	Secukinumab 300 mg every 4 weeks (Q4W) (safety)

Arm description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.

Arm type	Active comparator
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details: Secukinumab 150 mg solution for subcutaneous (sc) injection in a 1 mL prefilled syringe (PFS)	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Placebo solution for sc injection in a 1 mL PFS matching the composition and appearance of secukinumab 150 mg dose	
Arm title	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)
Arm description: 2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).	
Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Placebo solution for sc injection in a 1 mL PFS matching the composition and appearance of secukinumab 150 mg dose	
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Secukinumab 150 mg solution for subcutaneous (sc) injection in a 1 mL prefilled syringe (PFS)	

Number of subjects in period 1	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (safety)	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)
Started	165	135	31
Completed	148	117	28
Not completed	17	18	3
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	5	5	1
Adverse event, non-fatal	4	8	2
Withdrawal of informed consent	2	1	-
Lost to follow-up	4	1	-
New therapy for study indication	1	-	-
Lack of efficacy	1	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 300 mg every 2 weeks (Q2W)
Reporting group description:	
2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	
Reporting group title	Secukinumab 300 mg every 4 weeks (Q4W) (safety)
Reporting group description:	
2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.	
Reporting group title	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)
Reporting group description:	
2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).	

Reporting group values	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (safety)	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)
Number of subjects	165	135	31
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)	145	126	29
From 65-84 years	20	9	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	48.2	46.1	44.7
standard deviation	± 12.73	± 13.24	± 13.61
Sex: Female, Male Units: participants			
Female	39	34	10
Male	126	101	21
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	0
Asian	4	4	1
Native Hawaiian or Other Pacific Islander	2	0	0

Black or African American	7	5	0
White	151	125	30
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	331		
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)	300		
From 65-84 years	31		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	83		
Male	248		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2		
Asian	9		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	12		
White	306		
More than one race	0		
Unknown or Not Reported	0		

Subject analysis sets

Subject analysis set title	Secukinumab 300 mg every 2 weeks (Q2W)
Subject analysis set type	Full analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.

Subject analysis set title	Secukinumab 300 mg Q4W (up to week 16 pre-dose)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received 2 injections of secukinumab 150 mg once weekly for four weeks (at Randomization, Weeks 1, 2 and 3), followed by 2 injections of secukinumab 150 mg every four weeks, starting at Week 4 and up to Week 12.

Subject analysis set title	Secukinumab 300 mg Q4W (safety)

Subject analysis set type	Safety analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.

Subject analysis set title	Secukinumab 300 mg Q4W (efficacy)
Subject analysis set type	Full analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes subjects randomized to remain on Q4W the entire treatment period, regardless of Psoriasis Area and Severity Index (PASI) 90 response status at Week 16.

Subject analysis set title	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)
Subject analysis set type	Full analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).

Reporting group values	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg Q4W (up to week 16 pre-dose)	Secukinumab 300 mg Q4W (safety)
Number of subjects	165	166	135
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years arithmetic mean standard deviation	 ±	 92 ±	 ±
Sex: Female, Male Units: participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Secukinumab 300 mg Q4W (efficacy)	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)	
Number of subjects	83	31	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	
Sex: Female, Male			
Units: participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	Secukinumab 300 mg every 2 weeks (Q2W)

Reporting group description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.

Reporting group title	Secukinumab 300 mg every 4 weeks (Q4W) (safety)

Reporting group description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.

Reporting group title	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)

Reporting group description:

2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).

Subject analysis set title	Secukinumab 300 mg every 2 weeks (Q2W)
Subject analysis set type	Full analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.

Subject analysis set title	Secukinumab 300 mg Q4W (up to week 16 pre-dose)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received 2 injections of secukinumab 150 mg once weekly for four weeks (at Randomization, Weeks 1, 2 and 3), followed by 2 injections of secukinumab 150 mg every four weeks, starting at Week 4 and up to Week 12.

Subject analysis set title	Secukinumab 300 mg Q4W (safety)
Subject analysis set type	Safety analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.

Subject analysis set title	Secukinumab 300 mg Q4W (efficacy)
Subject analysis set type	Full analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes subjects randomized to remain on Q4W the entire treatment period, regardless of Psoriasis Area and Severity Index (PASI) 90 response status at Week 16.

Subject analysis set title	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)
Subject analysis set type	Full analysis

Subject analysis set description:

2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).

Primary: Number of subjects who achieve 90% or greater reduction in Psoriasis Area and Severity Index (PASI) score – week 16 (Full analysis set)

End point title	Number of subjects who achieve 90% or greater reduction in Psoriasis Area and Severity Index (PASI) score – week 16 (Full analysis set)

End point description:

A subject was considered as a PASI 90 responder if s/he achieved a reduction of 90% or more of the PASI score, compared to baseline, at a given time point.The head, trunk, upper limbs and lower limbs were assessed separately for erythema, thickening, and scaling. PASI scores can range from a lower value of 0, corresponding to no signs of psoriasis, up to a theoretic maximum of 72.0, i.e., higher scores represent more severity.

End point type	Primary

End point timeframe:

16 weeks

End point values	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg Q4W (up to week 16 pre-dose)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	166		
Units: Participants	121	92		

Statistical analyses

Statistical analysis title	Analysis of PASI 90 response at Week 16
Comparison groups	Secukinumab 300 mg every 2 weeks (Q2W) v Secukinumab 300 mg Q4W (up to week 16 pre-dose)
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003 [1]
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	17.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.45
upper limit	27.98

Notes:

[1] - One-sided p-value

Statistical analysis title	Analysis of PASI 90 response at Week 16
Comparison groups	Secukinumab 300 mg every 2 weeks (Q2W) v Secukinumab 300 mg Q4W (up to week 16 pre-dose)

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	3.78

Notes:

[2] - One-sided p-value

Secondary: Number of subjects who achieve Investigator Global Assessment (IGA modified 2011) score of 0 or 1 - week 16 (Full analysis set)

End point title	Number of subjects who achieve Investigator Global Assessment (IGA modified 2011) score of 0 or 1 - week 16 (Full analysis set)

End point description:

IGA mod 2011 was conducted for overall psoriatic disease. The IGA modified 2011 used in this study was static, i.e., it referred exclusively to the subject's disease state at the time of the assessments, and did not attempt a comparison with any of the subject's previous disease states, whether at baseline or at a previous visit. The scale has 0 (clear) as min and 4 (severe) as max, i.e., a higher score indicates more severity.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg Q4W (up to week 16 pre-dose)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	166		
Units: Participants	122	109		

Statistical analyses

Statistical analysis title	Analysis of PASI 90 response at Week 16
Comparison groups	Secukinumab 300 mg every 2 weeks (Q2W) v Secukinumab 300 mg Q4W (up to week 16 pre-dose)

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0498 [3]
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	8.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	18.2

Notes:

[3] - One-sided p-value

Statistical analysis title	Analysis of PASI 90 response at Week 16
Comparison groups	Secukinumab 300 mg every 2 weeks (Q2W) v Secukinumab 300 mg Q4W (up to week 16 pre-dose)
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0498 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	2.47

Notes:

[4] - One-sided p-value

Secondary: Absolute and relative frequencies for deaths, other serious or clinically significant adverse events or related discontinuations - Entire Study Period (Safety set)

End point title	Absolute and relative frequencies for deaths, other serious or clinically significant adverse events or related discontinuations - Entire Study Period (Safety set)

End point description:

An adverse event (AE) is any untoward medical occurrence (e.g., any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study until the end of study visit. Therefore, an AE may or may not be temporally or causally associated with the use of a medicinal (investigational) product.

End point type	Secondary

End point timeframe:

Adverse events were reported from first dose of study treatment until end of study treatment plus 8 weeks post treatment, up to a maximum timeframe of 470 days.

End point values	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (safety)	Secukinumab 300 mg Q4W non-responders up-titration (Q4W NR up)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	165	134	31	
Units: Participants				
Participants with any AE(s)	127	97	24	
Participants with SAE of Death	0	1	0	
Participants with Non-fatal SAE(s)	14	17	4	
Participants who disc. study treatment due to AE	4	9	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 8 weeks post treatment, up to a maximum timeframe of 470 days.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Secukinumab 300 mg every 2 weeks (Q2W)

Reporting group description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.

Reporting group title	Secukinumab 300 mg Q4W (safety)

Reporting group description:

2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.

Reporting group title	Secukinumab 300 mg Q$W non-responders up-titration (Q4W NR up)

Reporting group description:

2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).

Reporting group title	All Patients

Reporting group description:

All Patients

Serious adverse events	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg Q4W (safety)	Secukinumab 300 mg Q$W non-responders up-titration (Q4W NR up)
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 165 (8.48%)	18 / 134 (13.43%)	4 / 31 (12.90%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Peripheral ischaemia			

subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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			
Asthenia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Non-cardiac chest pain			
subjects affected / exposed	2 / 165 (1.21%)	0 / 134 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 165 (0.61%)	1 / 134 (0.75%)	0 / 31 (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
Epistaxis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Sleep apnoea syndrome			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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			
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Lipase increased			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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			
Blast injury			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Fall			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Ligament rupture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Multiple injuries			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Periprosthetic fracture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Procedural pain			

subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Road traffic accident			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Atrial fibrillation			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Diastolic dysfunction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Tachycardia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Quadriplegia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Ear and labyrinth disorders			

Deafness			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Tinnitus			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Dysphagia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Inguinal hernia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 134 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal mass			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Umbilical hernia, obstructive			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 165 (0.00%)	0 / 134 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholestatic liver injury			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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			
Cervical spinal stenosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Fibromyalgia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Rotator cuff syndrome			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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
Infections and infestations			
Acute HIV infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Breast cellulitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Endocarditis bacterial			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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

Erysipelas			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Pneumonia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 134 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 165 (0.00%)	2 / 134 (1.49%)	0 / 31 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Tooth abscess			
subjects affected / exposed	0 / 165 (0.00%)	0 / 134 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	0 / 31 (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
Diabetic ketoacidosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	0 / 31 (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

Serious adverse events	All Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 330 (10.91%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		

Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	2 / 330 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 330 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Blast injury				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	2 / 330 (0.61%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Joint injury				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periprosthetic fracture				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Procedural pain				

subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Atrial fibrillation			
subjects affected / exposed	2 / 330 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Diastolic dysfunction			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	2 / 330 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Quadriplegia			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			

Deafness			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tinnitus			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal mass			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia, obstructive			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 330 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cholestatic liver injury				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Cervical spinal stenosis				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fibromyalgia				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acute HIV infection				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Breast cellulitis				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocarditis bacterial				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Erysipelas				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 330 (0.61%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tooth abscess				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 330 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg Q4W (safety)	Secukinumab 300 mg Q$W non-responders up-titration (Q4W NR up)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 165 (40.00%)	57 / 134 (42.54%)	16 / 31 (51.61%)
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 165 (0.61%)	3 / 134 (2.24%)	3 / 31 (9.68%)
occurrences (all)	1	3	4
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 165 (0.00%)	1 / 134 (0.75%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 165 (6.67%)	6 / 134 (4.48%)	1 / 31 (3.23%)
occurrences (all)	13	6	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 165 (2.42%)	3 / 134 (2.24%)	2 / 31 (6.45%)
occurrences (all)	4	3	2
Pyrexia			
subjects affected / exposed	2 / 165 (1.21%)	2 / 134 (1.49%)	2 / 31 (6.45%)
occurrences (all)	2	3	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 165 (6.06%)	6 / 134 (4.48%)	2 / 31 (6.45%)
occurrences (all)	12	8	2
Nausea			
subjects affected / exposed	1 / 165 (0.61%)	4 / 134 (2.99%)	2 / 31 (6.45%)
occurrences (all)	1	5	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 165 (4.24%)	2 / 134 (1.49%)	2 / 31 (6.45%)
occurrences (all)	8	2	3
Oropharyngeal pain			

subjects affected / exposed	3 / 165 (1.82%)	7 / 134 (5.22%)	2 / 31 (6.45%)
occurrences (all)	3	7	2
Skin and subcutaneous tissue disorders			
Intertrigo			
subjects affected / exposed	4 / 165 (2.42%)	0 / 134 (0.00%)	3 / 31 (9.68%)
occurrences (all)	4	0	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 165 (4.24%)	6 / 134 (4.48%)	2 / 31 (6.45%)
occurrences (all)	8	6	2
Back pain			
subjects affected / exposed	3 / 165 (1.82%)	6 / 134 (4.48%)	2 / 31 (6.45%)
occurrences (all)	3	7	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	32 / 165 (19.39%)	22 / 134 (16.42%)	5 / 31 (16.13%)
occurrences (all)	46	27	7
Tooth abscess			
subjects affected / exposed	1 / 165 (0.61%)	0 / 134 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	12 / 165 (7.27%)	9 / 134 (6.72%)	3 / 31 (9.68%)
occurrences (all)	15	11	4
Urinary tract infection			
subjects affected / exposed	1 / 165 (0.61%)	5 / 134 (3.73%)	2 / 31 (6.45%)
occurrences (all)	1	6	2
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	3 / 165 (1.82%)	0 / 134 (0.00%)	2 / 31 (6.45%)
occurrences (all)	3	0	2

Non-serious adverse events	All Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 330 (42.12%)		
Investigations			
Neutrophil count decreased			

subjects affected / exposed occurrences (all)	7 / 330 (2.12%) 8		
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	 3 / 330 (0.91%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 18 / 330 (5.45%) 20		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 9 / 330 (2.73%) 9 6 / 330 (1.82%) 8		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 18 / 330 (5.45%) 22 7 / 330 (2.12%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 11 / 330 (3.33%) 13 12 / 330 (3.64%) 12		
Skin and subcutaneous tissue disorders Intertrigo subjects affected / exposed occurrences (all)	 7 / 330 (2.12%) 7		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	15 / 330 (4.55%)		
occurrences (all)	16		
Back pain			
subjects affected / exposed	11 / 330 (3.33%)		
occurrences (all)	12		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	59 / 330 (17.88%)		
occurrences (all)	80		
Tooth abscess			
subjects affected / exposed	3 / 330 (0.91%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	24 / 330 (7.27%)		
occurrences (all)	30		
Urinary tract infection			
subjects affected / exposed	8 / 330 (2.42%)		
occurrences (all)	9		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	5 / 330 (1.52%)		
occurrences (all)	5		

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? Yes

Date	Interruption	Restart date
08 February 2019	The study was temporarily interrupted because of insufficient drug supply. New supply was released in the US on 06 March 2019 and in Canada and Russia on 07 Mar 2019.	06 March 2019

Notes:

Limitations and caveats

None reported