Clinical trial results:
An open-label, prospective, non-randomized, multicenter study to evaluate clear skin effect on health-related quality of life outcomes at 16 and 52 weeks in patients with moderate to severe plaque psoriasis treated with secukinumab 300 mg s.c. with or without previous exposure to systemic therapy

Summary

EudraCT number	2015-003701-42
Trial protocol	ES DE GB BE LV PT SK LT PL GR RO IT
Global end of trial date	28 March 2018

Results information

Result version number	v1 (current)
This version publication date	06 April 2019
First version publication date	06 April 2019

Trial information

Trial identification

Sponsor protocol code	CAIN457A3401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02752776
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Manager, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Manager, 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	28 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the proportion of patients achieving a Dermatology Life Quality Index (DLQI) 0/1 response at Week 16 in 3 pre-defined subpopulations and in the overall study population.

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	17 March 2016
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	Belgium: 20
Country: Number of subjects enrolled	Bulgaria: 25
Country: Number of subjects enrolled	Czech Republic: 33
Country: Number of subjects enrolled	Estonia: 46
Country: Number of subjects enrolled	France: 297
Country: Number of subjects enrolled	Germany: 506
Country: Number of subjects enrolled	United Kingdom: 108
Country: Number of subjects enrolled	Greece: 16
Country: Number of subjects enrolled	Israel: 30
Country: Number of subjects enrolled	Italy: 40
Country: Number of subjects enrolled	Latvia: 34
Country: Number of subjects enrolled	Lithuania: 32
Country: Number of subjects enrolled	Poland: 148
Country: Number of subjects enrolled	Portugal: 34
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Slovakia: 31
Country: Number of subjects enrolled	Spain: 239
Worldwide total number of subjects	1660
EEA total number of subjects	1630

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)	1524
From 65 to 84 years	134
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

A total of 1660 participants were treated and included in the Safety set.

Pre-assignment

Screening details:

A total of 1858 patients were screened in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Subpopulation A (naive)

Arm description:

Subjects who were naïve to any systemic treatment, e.g. participants failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment.

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

secukinumab/AIN457 300 mg s.c. as per EU SmPC. Secukinumab 300 mg (2 × PFS of the 150 mg dose) was self-administered by the patient (or caregiver).

Arm title	Subpopulation B (non-biologic)

Arm description:

Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment.

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

secukinumab/AIN457 300 mg s.c. as per EU SmPC. Secukinumab 300 mg (2 × PFS of the 150 mg dose) was self-administered by the patient (or caregiver).

Arm title	Subpopulation C (biologic)

Arm description:

Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment.

Arm type	Experimental

Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

secukinumab/AIN457 300 mg s.c. as per EU SmPC. Secukinumab 300 mg (2 × PFS of the 150 mg dose) was self-administered by the patient (or caregiver).

Number of subjects in period 1	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)
Started	663	673	324
Full Analysis Set	662	673	324
Completed	611	597	276
Not completed	52	76	48
Adverse event, serious fatal	-	-	1
Physician decision	2	6	2
Consent withdrawn by subject	3	4	2
Adverse event, non-fatal	15	23	11
Non-compliance with study treatment	-	-	1
Pregnancy	1	6	3
Lost to follow-up	11	12	4
Subject/guardian decision	8	6	4
Lack of efficacy	2	6	14
Protocol deviation	10	13	6

Baseline characteristics

Reporting groups	
Reporting group title	Subpopulation A (naive)
Reporting group description:	
Subjects who were naïve to any systemic treatment, e.g. participants failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment.	
Reporting group title	Subpopulation B (non-biologic)
Reporting group description:	
Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment.	
Reporting group title	Subpopulation C (biologic)
Reporting group description:	
Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment.	

Reporting group values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)
Number of subjects	663	673	324
Age categorical Units: Subjects			
Adults (18-64 years)	617	617	290
From 65-84 years	44	56	34
85 years and over	2	0	0
Age Continuous Units: years			
arithmetic mean	43.2	44.4	47.4
standard deviation	± 14.03	± 13.67	± 12.89
Sex: Female, Male Units: Subjects			
Female	224	222	107
Male	439	451	217
Race/Ethnicity, Customized Units: Subjects			
Caucasian	626	642	307
Black	3	2	0
Asian	12	6	2
Other	22	23	15

Reporting group values	Total		
Number of subjects	1660		
Age categorical Units: Subjects			
Adults (18-64 years)	1524		
From 65-84 years	134		
85 years and over	2		

Age Continuous Units: years arithmetic mean standard deviation	- 		
Sex: Female, Male Units: Subjects			
Female	553		
Male	1107		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	1575		
Black	5		
Asian	20		
Other	60		

End points

End points reporting groups

Reporting group title	Subpopulation A (naive)

Reporting group description:

Subjects who were naïve to any systemic treatment, e.g. participants failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment.

Reporting group title	Subpopulation B (non-biologic)

Reporting group description:

Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment.

Reporting group title	Subpopulation C (biologic)

Reporting group description:

Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment.

Subject analysis set title	All Subjects - Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects from all 3 subpopulations: Subpopulation A B & C combined

Primary: Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 16

End point title	Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 16[1]

End point description:

Assessed the percentage of participants who achieved a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 16 in 3 pre-defined subpopulations and in the overall study population.

End point type	Primary

End point timeframe:

16 weeks

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: No statistical analysis was planned for this endpoint

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: Percentage of participants				
number (confidence interval 95%)	74.7 (71.2 to 78.0)	71.3 (67.7 to 74.7)	61.7 (56.1 to 67.0)	70.8 (68.5 to 73.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 52

End point title	Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 52

End point description:

Assessed the percentage of participants who achieved a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 52 in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: Percentage of participants				
number (confidence interval 95%)	75.3 (71.7 to 78.5)	73.3 (69.8 to 76.6)	62.0 (56.5 to 67.3)	71.9 (69.6 to 74.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in each DLQI score category at Week 16 and Week 52

End point title	Percentage of participants in each DLQI score category at Week 16 and Week 52

End point description:

Assessed the percentage of participants with Dermatology life quality index scores at Week 16 & 52 in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

52 weeks

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: Percentage of participants				
number (confidence interval 95%)				
Wk 16: DLQI cat. score: 2-5 (n=649,666,321,1636)	18.3 (15.5 to 21.6)	19.1 (16.2 to 22.3)	21.2 (16.9 to 26.2)	19.2 (17.3 to 21.2)
Wk 16: DLQI cat. score: 6-10 (n=649,666,321,1636)	5.7 (4.1 to 7.8)	6.3 (4.6 to 8.5)	9.3 (6.5 to 13.2)	6.7 (5.5 to 8.0)

Wk 16: DLQI cat. score: 11-20 (n=649,666,321,1636)	1.2 (0.6 to 2.5)	2.9 (1.8 to 4.5)	5.3 (3.2 to 8.5)	2.7 (2.0 to 3.6)
Wk 16: DLQI cat. score: 21-30 (n=649, 666,321,636)	0.0 (0.0 to 0.7)	0.5 (0.1 to 1.4)	2.5 (1.2 to 5.0)	0.7 (0.4 to 1.2)
Wk 52: DLQI cat. score: 2-5 (n=655,671,324,1650)	17.9 (15.0 to 21.1)	14.0 (11.5 to 16.9)	18.2 (14.2 to 23.0)	16.4 (14.6 to 18.3)
Wk 52: DLQI cat. score: 6-10 (n=655,671,324,1650)	4.7 (3.3 to 6.7)	7.2 (5.4 to 9.4)	9.6 (6.7 to 13.4)	6.7 (5.5 to 8.0)
Wk 52: DLQI cat. score: 11-20 (n=655 671,324,1650)	1.8 (1.0 to 3.3)	4.0 (2.7 to 5.9)	8.3 (5.7 to 12.0)	4.0 (3.1 to 5.1)
Wk 52: DLQI cat. score: 21-30 (n=655,671,324,1650)	0.3 (0.1 to 1.2)	1.5 (0.8 to 2.8)	1.9 (0.8 to 4.2)	1.1 (0.7 to 1.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with PASI 50, PASI 75, PASI 90, PASI 100 or IGA mod 2011 0/1 response at Week 16 and 52

End point title	Percentage of participants with PASI 50, PASI 75, PASI 90, PASI 100 or IGA mod 2011 0/1 response at Week 16 and 52

End point description:

Assed the percentage of participants who achieved PASI 50, PASI 75, PASI 90, PASI 100 and investigator's global assessment (IGA) mod 2011 0/1 responses at Week 16 and Week 52 in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

Week 16, Week 52

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: Percentage of participants				
number (confidence interval 95%)				
Wk 16: PASI 50 (n = 658, 670, 323, 1651)	97.7 (96.2 to 98.7)	97.5 (95.9 to 98.5)	95.0 (91.9 to 97.2)	97.1 (96.1 to 97.8)
Wk 16: PASI 75 (n = 658, 670, 323, 1651)	94.4 (92.3 to 96.0)	92.8 (90.5 to 94.7)	85.4 (81.0 to 89.1)	92.0 (90.6 to 93.3)
Wk 16: PASI 90 (n = 658, 670, 323, 1651)	82.4 (79.2 to 85.2)	78.8 (75.5 to 81.8)	69.0 (63.6 to 74.0)	78.3 (76.2 to 80.3)
Wk 16: PASI 100 (n = 658, 670, 323, 1651)	47.3 (43.4 to 51.2)	38.8 (35.1 to 42.6)	33.4 (28.4 to 38.9)	41.1 (38.7 to 43.6)
Wk 16: IGA 01 (n = 658, 671, 323, 1651)	87.4 (84.5 to 89.8)	84.9 (82.0 to 87.5)	76.2 (71.1 to 80.7)	84.2 (82.3 to 85.9)
Wk 52: PASI 50	97.9 (96.4 to 98.9)	96.3 (94.5 to 97.6)	92.9 (89.4 to 95.5)	96.3 (95.2 to 97.1)
Wk 52: PASI 75	94.4 (92.3 to 96.0)	89.7 (87.1 to 91.9)	83.3 (78.7 to 87.2)	90.4 (88.8 to 91.7)
Wk 52: PASI 90	80.8 (77.6 to 83.7)	75.5 (72.0 to 78.7)	63.9 (58.4 to 69.1)	75.3 (73.2 to 77.4)

Wk 52: PASI 100	56.9 (53.1 to 60.8)	45.5 (41.7 to 49.3)	37.0 (31.8 to 42.6)	48.4 (46.0 to 50.8)
Wk 52: IGA 0/1	86.4 (83.5 to 88.9)	79.9 (76.7 to 82.9)	71.3 (66.0 to 76.1)	80.8 (78.8 to 82.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in EQ-5D-5L crosswalk index at Week 16 and Week 52

End point title	Absolute change from baseline in EQ-5D-5L crosswalk index at Week 16 and Week 52

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in EuroQOL 5-Dimension Health Questionnaire (EQ-5D©) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

Week 16, Week 52

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 16 (n = 643, 656, 314, 1613)	0.217 (± 0.2294)	0.201 (± 0.2277)	0.235 (± 0.2602)	0.214 (± 0.2352)
Week 52 (n = 647, 659, 317, 1623)	0.221 (± 0.2353)	0.193 (± 0.2360)	0.226 (± 0.2596)	0.211 (± 0.2408)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in EQ-5D-5L visual analogue scale (VAS) at Week 16 and Week 52

End point title	Absolute change from baseline in EQ-5D-5L visual analogue scale (VAS) at Week 16 and Week 52

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in EuroQOL 5-Dimension Health Questionnaire (EQ-5D©) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

Week 16, Week 52

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 16 (n = 644, 656, 314, 1614)	19.7 (± 24.36)	21.4 (± 25.66)	18.7 (± 26.66)	20.2 (± 25.36)
Week 52 (n = 647, 659, 317, 1623)	21.7 (± 24.11)	22.6 (± 25.47)	19.5 (± 25.14)	21.7 (± 24.88)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in HAQ-DI at Week 16 and Week 52

End point title	Absolute change from baseline in HAQ-DI at Week 16 and Week 52

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in Health assessment questionnaire disability index (HAQ©-DI) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

Week 16 and Week 52

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	117	90	251
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 16 (n = 43, 109, 87, 239)	-0.7 (± 0.97)	-0.5 (± 0.83)	-0.3 (± 0.85)	-0.5 (± 0.87)
Week 52 (n = 44, 110, 88, 242)	-0.7 (± 0.90)	-0.5 (± 0.90)	-0.4 (± 0.85)	-0.5 (± 0.88)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in Numeric rating scale (NRS) at Week 16 and Week 52

End point title	Absolute change from baseline in Numeric rating scale (NRS) at Week 16 and Week 52

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in Numeric rating scale: patient's assessment of pain, itching and scaling response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

16 and 52 weeks

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: scores on a scale				
arithmetic mean (standard deviation)				
Pain: Wk 16 (n = 640, 649, 310, 1599)	-3.0 (± 2.87)	-3.3 (± 3.11)	-3.3 (± 3.30)	-3.2 (± 3.06)
Pain: Wk 52 (n = 645, 657, 316, 1618)	-3.1 (± 2.95)	-3.2 (± 3.22)	-3.3 (± 3.36)	-3.2 (± 3.14)
Itching: Wk 16 (n = 640, 649, 311, 1600)	-4.9 (± 2.96)	-4.9 (± 3.06)	-4.8 (± 3.31)	-4.9 (± 3.07)
Itching: Wk 52 (n = 646, 656, 317, 1619)	-5.0 (± 2.92)	-5.0 (± 3.10)	-4.6 (± 3.28)	-4.9 (± 3.07)
Scaling: Wk 16 (n = 640, 650, 312, 1602)	-5.5 (± 2.68)	-5.5 (± 2.71)	-5.2 (± 3.26)	-5.4 (± 2.81)
Scaling: Wk 52 (n = 646, 657, 317, 1620)	-5.4 (± 2.72)	-5.3 (± 2.87)	-4.9 (± 3.27)	-5.3 (± 2.90)

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Satisfaction Questionnaire for Medication (TSQM) scale scores at Week 16 and Week 52

End point title	Treatment Satisfaction Questionnaire for Medication (TSQM) scale scores at Week 16 and Week 52

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in TSQM scale scores (Effectiveness, Convenience, Global satisfaction scores) over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

16 and 52 weeks

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: scores on a scale				
arithmetic mean (standard deviation)				
Effectiveness: Wk 16 (n = 650, 668, 318, 1636)	81.5 (± 24.02)	80.9 (± 25.13)	75.0 (± 23.43)	80.8 (± 24.48)
Effectiveness: Wk 52 (n = 655, 671, 322, 1648)	85.1 (± 20.64)	82.0 (± 25.05)	74.9 (± 24.24)	81.9 (± 23.50)
Convenience: Wk 16 (n = 650, 668, 319, 1637)	79.2 (± 15.50)	80.8 (± 15.83)	75.9 (± 15.20)	79.2 (± 15.67)
Convenience: Wk 52 (n = 655, 671, 323, 1649)	82.8 (± 15.67)	83.9 (± 15.42)	78.9 (± 15.14)	82.5 (± 15.57)
Global satisfaction: Wk 16 (n=650,668,319,1637)	83.8 (± 14.71)	83.3 (± 16.68)	75.1 (± 20.07)	81.9 (± 16.99)
Global satisfaction: Wk 52 (n=655,671,322,1648)	83.9 (± 17.23)	81.9 (± 20.38)	73.5 (± 23.10)	81.1 (± 20.14)

Statistical analyses

No statistical analyses for this end point

Secondary: Patient benefit index (PBI) at Week 16 and Week 52

End point title	Patient benefit index (PBI) at Week 16 and Week 52

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in Patient benefit index (PBI) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

End point type	Secondary

End point timeframe:

Week 16 and Week 52

End point values	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)	All Subjects - Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	662	673	324	1659
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 16 (n = 439, 472, 226, 1137)	3.5 (± 0.61)	3.4 (± 0.69)	3.2 (± 0.85)	3.4 (± 0.70)
Week 52 (n= 509, 532, 253, 1294)	3.5 (± 0.70)	3.4 (± 0.80)	3.2 (± 0.96)	3.4 (± 0.80)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

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	20.1

Reporting groups

Reporting group title	Subpopulation A (naive)

Reporting group description:

Subjects who were naïve to any systemic treatment, e.g. subjects failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment.

Reporting group title	Subpopulation B (non-biologic)

Reporting group description:

Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or
intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment.

Reporting group title	Subpopulation C (biologic)

Reporting group description:

Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they
were in a need of a different biologic systemic treatment.

Reporting group title	All Subjects

Reporting group description:

Subjects from all 3 subpopulations: Subpopulation
A B & C combined.

Serious adverse events	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 663 (6.49%)	44 / 673 (6.54%)	32 / 324 (9.88%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			

subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (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
Bronchial carcinoma			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Gastrointestinal tract adenoma			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Malignant melanoma			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Pituitary tumour benign			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Seborrhoeic keratosis			

subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Thyroid cancer			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 663 (0.30%)	0 / 673 (0.00%)	0 / 324 (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
Hypovolaemic shock			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Erectile dysfunction			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Dyspnoea			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (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
Pharyngeal cyst			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Vocal cord leukoplakia			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Suicidal ideation			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Suicide attempt			

subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (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
Concussion			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Fall			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Head injury			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Humerus fracture			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Lower limb fracture			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (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
Lumbar vertebral fracture			

subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	2 / 324 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural dizziness			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Radius fracture			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Skin abrasion			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Tendon rupture			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Upper limb fracture			
subjects affected / exposed	0 / 663 (0.00%)	2 / 673 (0.30%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Angina pectoris			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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 failure			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Coronary artery disease			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Left ventricular failure			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Myocardial infarction			

subjects affected / exposed	2 / 663 (0.30%)	2 / 673 (0.30%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Ventricular fibrillation			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Nervous system disorders			
Carotid arteriosclerosis			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Cerebral infarction			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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 hyperglycaemic coma			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Dysaesthesia			

subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Facial paralysis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Ischaemic stroke			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	3 / 324 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Radiculopathy			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Transient ischaemic attack			

subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Pupils unequal			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Abdominal pain upper			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Colitis ulcerative			
subjects affected / exposed	2 / 663 (0.30%)	0 / 673 (0.00%)	0 / 324 (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
Constipation			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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

Crohn's disease			
subjects affected / exposed	1 / 663 (0.15%)	3 / 673 (0.45%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	1 / 1	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Functional gastrointestinal disorder			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Haemorrhoids			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Ileus paralytic			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Oedematous pancreatitis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Hepatic cirrhosis			

subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Erythema multiforme			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Pruritus			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Psoriasis			
subjects affected / exposed	1 / 663 (0.15%)	2 / 673 (0.30%)	2 / 324 (0.62%)
occurrences causally related to treatment / all	1 / 1	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			

subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	2 / 324 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Urinary retention			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 663 (0.15%)	2 / 673 (0.30%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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 pain			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Osteitis			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Osteoarthritis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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	1 / 663 (0.15%)	1 / 673 (0.15%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermo-hypodermitis			

subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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	4 / 663 (0.60%)	2 / 673 (0.30%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	1 / 4	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Gastroenteritis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Oral candidiasis			

subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Otitis media chronic			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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	1 / 663 (0.15%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purulent discharge			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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
Pyelonephritis			
subjects affected / exposed	1 / 663 (0.15%)	1 / 673 (0.15%)	0 / 324 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Septic shock			

subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tinea pedis			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 663 (0.00%)	2 / 673 (0.30%)	0 / 324 (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
Urinary tract infection			
subjects affected / exposed	1 / 663 (0.15%)	0 / 673 (0.00%)	0 / 324 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 663 (0.00%)	1 / 673 (0.15%)	0 / 324 (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	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 3 diabetes mellitus			
subjects affected / exposed	0 / 663 (0.00%)	0 / 673 (0.00%)	1 / 324 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	119 / 1660 (7.17%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bladder transitional cell carcinoma			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchial carcinoma			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal tract adenoma			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pituitary tumour benign			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Seborrhoeic keratosis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertension				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Varicose vein				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erectile dysfunction			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pharyngeal cyst				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vocal cord leukoplakia				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Alcohol abuse				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Alcohol withdrawal syndrome				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			

subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Procedural dizziness				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin abrasion				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	3 / 1660 (0.18%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				

subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Left ventricular failure				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	4 / 1660 (0.24%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular fibrillation				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carotid arteriosclerosis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic hyperglycaemic coma				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic neuropathy				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysaesthesia				

subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial paralysis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial aneurysm				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	3 / 1660 (0.18%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radiculopathy				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Pupils unequal			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vitreous haemorrhage			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Crohn's disease				
subjects affected / exposed	4 / 1660 (0.24%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Food poisoning				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Functional gastrointestinal disorder				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedematous pancreatitis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic cirrhosis				

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Drug eruption			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erythema multiforme			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pruritus			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psoriasis			
subjects affected / exposed	5 / 1660 (0.30%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			

subjects affected / exposed	3 / 1660 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bursitis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	3 / 1660 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal pain				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteitis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	2 / 1660 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	3 / 1660 (0.18%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 1660 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dermo-hypodermitis				

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	6 / 1660 (0.36%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes virus infection			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Necrotising fasciitis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media chronic			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Post procedural infection			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Purulent discharge			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection viral			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			

subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tinea pedis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	2 / 1660 (0.12%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 3 diabetes mellitus			
subjects affected / exposed	1 / 1660 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Subpopulation A (naive)	Subpopulation B (non-biologic)	Subpopulation C (biologic)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	450 / 663 (67.87%)	474 / 673 (70.43%)	203 / 324 (62.65%)
Vascular disorders			
Hypertension			
subjects affected / exposed	26 / 663 (3.92%)	31 / 673 (4.61%)	8 / 324 (2.47%)
occurrences (all)	29	34	8
Nervous system disorders			
Headache			
subjects affected / exposed	76 / 663 (11.46%)	79 / 673 (11.74%)	21 / 324 (6.48%)
occurrences (all)	180	133	31
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	16 / 663 (2.41%)	10 / 673 (1.49%)	7 / 324 (2.16%)
occurrences (all)	19	12	9
Fatigue			
subjects affected / exposed	17 / 663 (2.56%)	25 / 673 (3.71%)	6 / 324 (1.85%)
occurrences (all)	25	29	7
Influenza like illness			
subjects affected / exposed	8 / 663 (1.21%)	15 / 673 (2.23%)	4 / 324 (1.23%)
occurrences (all)	8	16	5
Pyrexia			
subjects affected / exposed	11 / 663 (1.66%)	12 / 673 (1.78%)	8 / 324 (2.47%)
occurrences (all)	11	13	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	35 / 663 (5.28%)	30 / 673 (4.46%)	14 / 324 (4.32%)
occurrences (all)	47	34	19
Toothache			
subjects affected / exposed	14 / 663 (2.11%)	15 / 673 (2.23%)	5 / 324 (1.54%)
occurrences (all)	15	16	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	37 / 663 (5.58%)	31 / 673 (4.61%)	12 / 324 (3.70%)
occurrences (all)	39	33	15
Oropharyngeal pain			

subjects affected / exposed	34 / 663 (5.13%)	40 / 673 (5.94%)	14 / 324 (4.32%)
occurrences (all)	38	47	15
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 663 (0.45%)	7 / 673 (1.04%)	8 / 324 (2.47%)
occurrences (all)	3	7	8
Eczema			
subjects affected / exposed	25 / 663 (3.77%)	20 / 673 (2.97%)	5 / 324 (1.54%)
occurrences (all)	27	24	5
Intertrigo			
subjects affected / exposed	12 / 663 (1.81%)	15 / 673 (2.23%)	3 / 324 (0.93%)
occurrences (all)	15	16	3
Pruritus			
subjects affected / exposed	31 / 663 (4.68%)	41 / 673 (6.09%)	13 / 324 (4.01%)
occurrences (all)	34	50	15
Psoriasis			
subjects affected / exposed	20 / 663 (3.02%)	36 / 673 (5.35%)	22 / 324 (6.79%)
occurrences (all)	25	40	25
Urticaria			
subjects affected / exposed	14 / 663 (2.11%)	7 / 673 (1.04%)	3 / 324 (0.93%)
occurrences (all)	15	7	4
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	10 / 663 (1.51%)	17 / 673 (2.53%)	5 / 324 (1.54%)
occurrences (all)	12	18	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 663 (3.92%)	28 / 673 (4.16%)	18 / 324 (5.56%)
occurrences (all)	30	34	25
Back pain			
subjects affected / exposed	31 / 663 (4.68%)	46 / 673 (6.84%)	15 / 324 (4.63%)
occurrences (all)	35	57	17
Myalgia			
subjects affected / exposed	10 / 663 (1.51%)	7 / 673 (1.04%)	7 / 324 (2.16%)
occurrences (all)	14	10	8
Pain in extremity			

subjects affected / exposed	15 / 663 (2.26%)	17 / 673 (2.53%)	7 / 324 (2.16%)
occurrences (all)	17	17	8
Tendonitis			
subjects affected / exposed	6 / 663 (0.90%)	1 / 673 (0.15%)	7 / 324 (2.16%)
occurrences (all)	7	1	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	24 / 663 (3.62%)	27 / 673 (4.01%)	10 / 324 (3.09%)
occurrences (all)	25	30	12
Conjunctivitis			
subjects affected / exposed	33 / 663 (4.98%)	21 / 673 (3.12%)	15 / 324 (4.63%)
occurrences (all)	42	26	19
Folliculitis			
subjects affected / exposed	16 / 663 (2.41%)	21 / 673 (3.12%)	7 / 324 (2.16%)
occurrences (all)	19	23	9
Gastroenteritis			
subjects affected / exposed	21 / 663 (3.17%)	14 / 673 (2.08%)	6 / 324 (1.85%)
occurrences (all)	22	14	6
Influenza			
subjects affected / exposed	15 / 663 (2.26%)	17 / 673 (2.53%)	8 / 324 (2.47%)
occurrences (all)	16	20	8
Nasopharyngitis			
subjects affected / exposed	189 / 663 (28.51%)	189 / 673 (28.08%)	66 / 324 (20.37%)
occurrences (all)	296	284	108
Oral candidiasis			
subjects affected / exposed	16 / 663 (2.41%)	30 / 673 (4.46%)	14 / 324 (4.32%)
occurrences (all)	23	41	16
Oral herpes			
subjects affected / exposed	16 / 663 (2.41%)	8 / 673 (1.19%)	7 / 324 (2.16%)
occurrences (all)	23	11	10
Otitis externa			
subjects affected / exposed	9 / 663 (1.36%)	7 / 673 (1.04%)	7 / 324 (2.16%)
occurrences (all)	10	8	7
Pharyngitis			
subjects affected / exposed	28 / 663 (4.22%)	19 / 673 (2.82%)	10 / 324 (3.09%)
occurrences (all)	33	21	11

Rhinitis			
subjects affected / exposed	37 / 663 (5.58%)	37 / 673 (5.50%)	11 / 324 (3.40%)
occurrences (all)	47	50	13
Sinusitis			
subjects affected / exposed	11 / 663 (1.66%)	16 / 673 (2.38%)	11 / 324 (3.40%)
occurrences (all)	11	19	14
Tinea pedis			
subjects affected / exposed	16 / 663 (2.41%)	18 / 673 (2.67%)	7 / 324 (2.16%)
occurrences (all)	16	18	7
Tonsillitis			
subjects affected / exposed	22 / 663 (3.32%)	34 / 673 (5.05%)	11 / 324 (3.40%)
occurrences (all)	29	39	14
Upper respiratory tract infection			
subjects affected / exposed	39 / 663 (5.88%)	25 / 673 (3.71%)	20 / 324 (6.17%)
occurrences (all)	51	29	23
Urinary tract infection			
subjects affected / exposed	26 / 663 (3.92%)	21 / 673 (3.12%)	13 / 324 (4.01%)
occurrences (all)	38	29	15

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1127 / 1660 (67.89%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	65 / 1660 (3.92%)		
occurrences (all)	71		
Nervous system disorders			
Headache			
subjects affected / exposed	176 / 1660 (10.60%)		
occurrences (all)	343		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	33 / 1660 (1.99%)		
occurrences (all)	40		
Fatigue			

subjects affected / exposed	48 / 1660 (2.89%)		
occurrences (all)	61		
Influenza like illness			
subjects affected / exposed	27 / 1660 (1.63%)		
occurrences (all)	29		
Pyrexia			
subjects affected / exposed	31 / 1660 (1.87%)		
occurrences (all)	34		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	79 / 1660 (4.76%)		
occurrences (all)	100		
Toothache			
subjects affected / exposed	34 / 1660 (2.05%)		
occurrences (all)	37		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	80 / 1660 (4.82%)		
occurrences (all)	87		
Oropharyngeal pain			
subjects affected / exposed	88 / 1660 (5.30%)		
occurrences (all)	100		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	18 / 1660 (1.08%)		
occurrences (all)	18		
Eczema			
subjects affected / exposed	50 / 1660 (3.01%)		
occurrences (all)	56		
Intertrigo			
subjects affected / exposed	30 / 1660 (1.81%)		
occurrences (all)	34		
Pruritus			
subjects affected / exposed	85 / 1660 (5.12%)		
occurrences (all)	99		
Psoriasis			

subjects affected / exposed	78 / 1660 (4.70%)		
occurrences (all)	90		
Urticaria			
subjects affected / exposed	24 / 1660 (1.45%)		
occurrences (all)	26		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	32 / 1660 (1.93%)		
occurrences (all)	37		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	72 / 1660 (4.34%)		
occurrences (all)	89		
Back pain			
subjects affected / exposed	92 / 1660 (5.54%)		
occurrences (all)	109		
Myalgia			
subjects affected / exposed	24 / 1660 (1.45%)		
occurrences (all)	32		
Pain in extremity			
subjects affected / exposed	39 / 1660 (2.35%)		
occurrences (all)	42		
Tendonitis			
subjects affected / exposed	14 / 1660 (0.84%)		
occurrences (all)	15		
Infections and infestations			
Bronchitis			
subjects affected / exposed	61 / 1660 (3.67%)		
occurrences (all)	67		
Conjunctivitis			
subjects affected / exposed	69 / 1660 (4.16%)		
occurrences (all)	87		
Folliculitis			
subjects affected / exposed	44 / 1660 (2.65%)		
occurrences (all)	51		
Gastroenteritis			

subjects affected / exposed	41 / 1660 (2.47%)			
occurrences (all)	42			
Influenza				
subjects affected / exposed	40 / 1660 (2.41%)			
occurrences (all)	44			
Nasopharyngitis				
subjects affected / exposed	444 / 1660 (26.75%)			
occurrences (all)	688			
Oral candidiasis				
subjects affected / exposed	60 / 1660 (3.61%)			
occurrences (all)	80			
Oral herpes				
subjects affected / exposed	31 / 1660 (1.87%)			
occurrences (all)	44			
Otitis externa				
subjects affected / exposed	23 / 1660 (1.39%)			
occurrences (all)	25			
Pharyngitis				
subjects affected / exposed	57 / 1660 (3.43%)			
occurrences (all)	65			
Rhinitis				
subjects affected / exposed	85 / 1660 (5.12%)			
occurrences (all)	110			
Sinusitis				
subjects affected / exposed	38 / 1660 (2.29%)			
occurrences (all)	44			
Tinea pedis				
subjects affected / exposed	41 / 1660 (2.47%)			
occurrences (all)	41			
Tonsillitis				
subjects affected / exposed	67 / 1660 (4.04%)			
occurrences (all)	82			
Upper respiratory tract infection				
subjects affected / exposed	84 / 1660 (5.06%)			
occurrences (all)	103			

Urinary tract infection subjects affected / exposed occurrences (all)	60 / 1660 (3.61%) 82		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported