



Clinical trial results:

A Phase 3b, Multicenter, Randomized, Blinded, Active-Controlled Study to Compare the Efficacy and safety of Ustekinumab to that of Adalimumab in the Treatment of Biologic Naïve Subjects with Moderately-to-Severely Active Crohn's Disease

Summary

EudraCT number	2017-004209-41
Trial protocol	ES CZ FR PL DE GB NL BG BE IT
Global end of trial date	21 May 2021

Results information

Result version number	v1 (current)
This version publication date	29 May 2022
First version publication date	29 May 2022

Trial information

Trial identification

Sponsor protocol code	CNT01275CRD3007
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03464136
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	Welsh & McKean Roads, Spring House, United States, PA 19477
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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	21 May 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to compare the efficacy of treatment with ustekinumab or adalimumab in biologic naïve subjects with moderately-to-severely active Crohn's disease (CD) who have previously failed or were intolerant to conventional therapy (corticosteroids and/or immunomodulators, that is, azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate [MTX]), as measured by clinical remission at one year.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety evaluations included adverse events (AEs), adverse events temporally related to infusion, clinical laboratory tests, and injection site reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 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	Australia: 7
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 23
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czechia: 22
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Poland: 60
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Russian Federation: 47
Country: Number of subjects enrolled	Serbia: 12
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 25

Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	386
EEA total number of subjects	180

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)	372
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 386 subjects (195 in the adalimumab group, and 191 in ustekinumab group) were randomized in this study and received the study drug. Out of 386 subjects, 331 subjects completed the study.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Adalimumab

Arm description:

Subjects received intravenous (IV) infusion of placebo for ustekinumab and 4 subcutaneous (SC) injections of adalimumab (each 40 milligrams [mg], total dose 160 mg) at Week 0, followed by 2 SC injections of adalimumab (each 40 mg, total dose 80 mg) at Week 2. From Week 4 to Week 56, subjects self-administered 1 SC injection of adalimumab 40 mg every 2 weeks (q2w).

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

Dosage and administration details:

Subjects received SC injections of adalimumab (each 40 mg, total dose 160 mg) at Week 0, followed by 2 SC injections of adalimumab (each 40 mg, total dose 80 mg) at Week 2. From Week 4 to Week 56, subjects self-administered 1 SC injection of adalimumab 40 mg.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received placebo as IV infusion to blind adalimumab.

Arm title	Ustekinumab
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Arm description:

Subjects received IV infusion of ustekinumab (approximately 6 milligram/kilogram [mg/kg]) and 4 SC injections of placebo for adalimumab at Week 0, followed by 2 SC injections of placebo at Week 2. From Week 4 to Week 56, subjects self-administered one SC injection of ustekinumab 90 mg every 8 weeks (q8w) starting at Week 8 and placebo for adalimumab at the other designated q2w dosing intervals.

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

Dosage and administration details:

Subjects self-administered SC injection of ustekinumab 90 mg.

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:

Subjects received placebo as as SC injection to blind ustekinumab.

Number of subjects in period 1	Adalimumab	Ustekinumab
Started	195	191
Completed	165	166
Not completed	30	25
Adverse event, serious fatal	1	-
Consent withdrawn by subject	16	13
Unspecified	8	4
Lost to follow-up	5	8

Baseline characteristics

Reporting groups

Reporting group title	Adalimumab
Reporting group description:	
Subjects received intravenous (IV) infusion of placebo for ustekinumab and 4 subcutaneous (SC) injections of adalimumab (each 40 milligrams [mg], total dose 160 mg) at Week 0, followed by 2 SC injections of adalimumab (each 40 mg, total dose 80 mg) at Week 2. From Week 4 to Week 56, subjects self-administered 1 SC injection of adalimumab 40 mg every 2 weeks (q2w).	
Reporting group title	Ustekinumab
Reporting group description:	
Subjects received IV infusion of ustekinumab (approximately 6 milligram/kilogram [mg/kg]) and 4 SC injections of placebo for adalimumab at Week 0, followed by 2 SC injections of placebo at Week 2. From Week 4 to Week 56, subjects self-administered one SC injection of ustekinumab 90 mg every 8 weeks (q8w) starting at Week 8 and placebo for adalimumab at the other designated q2w dosing intervals.	

Reporting group values	Adalimumab	Ustekinumab	Total
Number of subjects	195	191	386
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	189	183	372
From 65 to 84 years	6	8	14
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	37.4	37	
standard deviation	± 12.99	± 13.23	-
Title for Gender Units: subjects			
Female	100	101	201
Male	95	90	185

End points

End points reporting groups

Reporting group title	Adalimumab
Reporting group description:	
Subjects received intravenous (IV) infusion of placebo for ustekinumab and 4 subcutaneous (SC) injections of adalimumab (each 40 milligrams [mg], total dose 160 mg) at Week 0, followed by 2 SC injections of adalimumab (each 40 mg, total dose 80 mg) at Week 2. From Week 4 to Week 56, subjects self-administered 1 SC injection of adalimumab 40 mg every 2 weeks (q2w).	
Reporting group title	Ustekinumab
Reporting group description:	
Subjects received IV infusion of ustekinumab (approximately 6 milligram/kilogram [mg/kg]) and 4 SC injections of placebo for adalimumab at Week 0, followed by 2 SC injections of placebo at Week 2. From Week 4 to Week 56, subjects self-administered one SC injection of ustekinumab 90 mg every 8 weeks (q8w) starting at Week 8 and placebo for adalimumab at the other designated q2w dosing intervals.	

Primary: Percentage of Subjects with Clinical Remission at Week 52

End point title	Percentage of Subjects with Clinical Remission at Week 52 ^[1]
End point description:	
Percentage of Subjects with clinical remission at Week 52 were assessed. Clinical remission was defined as a Crohn's Disease Activity Index (CDAI) score of less than (<) 150 points (in general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities). The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. A decrease in CDAI over time indicates improvement in disease activity. Full analysis set (FAS) included all randomized subjects.	
End point type	Primary
End point timeframe:	
Week 52	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)	61.0	64.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Corticosteroid-free Remission at Week 52

End point title	Percentage of Subjects with Corticosteroid-free Remission at Week 52
End point description:	
Percentage of subjects with Corticosteroid-free remission at Week 52 were assessed. Corticosteroid-free remission was defined as CDAI score <150 points at Week 52 and not taking any corticosteroids for at	

least 30 days prior to Week 52. The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.

End point type	Secondary
End point timeframe:	
Week 52	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)	57.4	60.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Response at Week 52

End point title	Percentage of Subjects with Clinical Response at Week 52
End point description:	
Percentage of subjects with clinical response at Week 52 were assessed. Clinical response through Week 52 was defined as a reduction from baseline in the CDAI score of ≥ 100 points or CDAI score < 150 . The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)	66.2	72.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects in Patient Reported Outcome (PRO)-2 Symptom Remission at Week 52

End point title	Percentage of Subjects in Patient Reported Outcome (PRO)-2 Symptom Remission at Week 52
End point description:	
<p>PRO2 evaluated 2 patient-reported symptoms: the frequency of liquid or soft stools (total number of soft/liquid stools in the last 7 days) and abdominal pain (on a 4-point scale where 0 = none, 1 = mild, 2 = moderate, 3 = severe). A weekly score was calculated for the liquid or soft stool frequency and a separate weekly score was calculated for abdominal pain, in each case based on daily symptom reporting. PRO-2 symptom remission was defined as an abdominal pain (AP) mean daily score at or below 1 and also stool frequency (SF) mean daily score at or below 3, that is, AP ≤1 and SF ≤3. PRO2 is a composite index consisting of weighted scoring of both variables. PRO-2 scores range from 0 to no upper limit with higher scores indicating more severe disease. FAS included all randomized subjects.</p>	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)	55.4	56.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Remission at Week 16

End point title	Percentage of Subjects with Clinical Remission at Week 16
End point description:	
<p>Percentage of subject with clinical remission (defined as CDAI <150 points) at Week 16 were assessed. Clinical remission was defined as a CDAI score of <150 points (in general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities). The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.</p>	
End point type	Secondary
End point timeframe:	
Week 16	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of Subject				
number (not applicable)	60	57.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Endoscopic Remission at Week 52

End point title	Percentage of Subjects with Endoscopic Remission at Week 52
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End point description:

Percentage of subjects with endoscopic remission at Week 52 were assessed. Endoscopic remission was defined as Simple Endoscopic Score for Crohn's Disease (SES-CD) score less than or equal to (\leq) 3, or SES-CD = 0 for subjects who entered the study with a SES-CD = 3 at Week 52. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis) each rated from 0 (best) to 3 (worst) in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total score is the sum of 4 endoscopic variable scores and ranges from 0 to 56, where higher scores indicate more severe disease. FAS among participants with SES-CD Score \geq 3 at Baseline.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	179		
Units: percentage of subjects				
number (not applicable)	30.7	28.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Remission Through Week 52

End point title	Percentage of Subjects with Clinical Remission Through Week 52
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End point description:

Percentage of subjects with clinical remission at each postbaseline visit through Week 52 were reported. Clinical remission was defined as a CDAI score of <150 points (in general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities). The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.

End point type	Secondary
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End point timeframe:

Weeks 2, 8, 16, 24, 32, 40, 48, and 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Week 2	28.7	23.0		
Week 8	47.7	50.3		
Week 16	60.0	57.1		
Week 24	66.2	57.6		
Week 32	65.1	59.7		
Week 40	60.5	64.9		
Week 48	59.0	62.8		
Week 52	61.0	64.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Response Through Week 52

End point title	Percentage of Subjects with Clinical Response Through Week 52
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End point description:

Percentage of subjects with clinical response at each postbaseline visit through Week 52 were reported. Clinical response through Week 52 was defined as a reduction from baseline in the CDAI score of ≥ 100 points or CDAI score < 150 . The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.

End point type	Secondary
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End point timeframe:

Weeks 2, 8, 16, 24, 32, 40, 48, and 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Week 2	46.2	38.2		
Week 8	66.2	68.1		
Week 16	72.3	73.3		
Week 24	76.4	70.7		
Week 32	74.9	71.2		
Week 40	69.2	74.3		
Week 48	66.7	69.1		
Week 52	66.2	72.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with Durable Clinical Response at Week 52

End point title	Percentage of subjects with Durable Clinical Response at Week 52
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End point description:

Percentage of subjects with durable clinical response at Week 52 were reported. Durable clinical response was defined as CDAI score decreased at least 100 from baseline or CDAI <150 at Week 52 and was $\geq 80\%$ of all visits between Week 16 and Week 52. The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)	60.5	65.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Durable Clinical Remission at Week 52

End point title	Percentage of Subjects with Durable Clinical Remission at Week 52
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End point description:

Percentage of subject with durable clinical remission at Week 52 were reported. Clinical remission was defined as CDAI score <150 at Week 52 and was $\geq 80\%$ of all visits between Week 16 and Week 52. The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)	51.8	50.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Abdominal Pain (AP) Improvement Through Week 52

End point title	Percentage of Subjects with Abdominal Pain (AP) Improvement Through Week 52
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End point description:

Percentage of subjects with AP improvement through Week 52 were reported. AP improvement was defined as at least 1 point or greater improvement in mean daily CDAI AP score (ranges from 0 to 3, where higher score indicates severity of pain) from baseline, or a mean score of zero among subjects with mean AP > 0 at baseline, compared at each visit through Week 52. FAS among subjects with mean daily AP Score > 0 at Baseline. Here 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Weeks 2, 8, 16, 24, 32, 40, 48, and 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	191		
Units: percentage of subjects				
number (not applicable)				
Week 2	29.9	23.0		
Week 8	54.1	53.9		
Week 16	62.9	59.2		
Week 24	66.5	61.8		
Week 32	63.9	63.9		
Week 40	60.3	63.9		
Week 48	61.9	61.8		
Week 52	62.4	64.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Reduction in Frequency of Diarrhea Through Week 52

End point title	Percentage of Subjects with Reduction in Frequency of Diarrhea Through Week 52
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End point description:

Percentage of subjects with reduction in frequency of diarrhea were reported. Reduction in frequency of diarrhea was defined as a reduction of at least 3 (or a mean number <1) in SF (that is, mean daily number of liquid or very soft stools from CDAI score [ranges from 0 to 3 where higher score indicates severity of pain] in the week prior to the visit) from baseline, among subjects with mean SF >1 at baseline, compared at each visit through Week 52. FAS among subjects with mean daily stool frequency >1 at baseline. Here 'N' (number of subjects analyzed) signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Weeks 2, 8, 16, 24, 32, 40, 48, and 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	179		
Units: percentage of subjects				
number (not applicable)				
Week 2	33.3	30.7		
Week 8	52.7	60.3		
Week 16	53.8	60.9		
Week 24	58.1	60.9		
Week 32	58.1	60.9		
Week 40	54.8	64.2		
Week 48	53.8	57.5		
Week 52	52.7	60.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical and Biomarker Remission at Weeks 8, 16 and 52

End point title	Percentage of Subjects with Clinical and Biomarker Remission at Weeks 8, 16 and 52
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End point description:

Percentage of subjects with clinical and biomarker remission was defined as the percentage of subjects with CDAI <150 , CRP ≤ 3 mg/L, and also fecal calprotectin ≤ 250 micrograms per gram (mcg/g). The CDAI score is used to quantify the symptoms of subjects with Crohn's Disease. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. A decrease in CDAI over time indicates improvement in disease activity. FAS included all randomized subjects.

End point type	Secondary
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End point timeframe:

At Weeks 8, 16 and 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Week 8	19.5	14.1		
Week 16	29.7	18.8		
Week 52	27.2	20.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Adverse Events (AEs)

End point title	Percentage of Subjects with Adverse Events (AEs)
End point description:	
Percentage of subjects with AE were reported. An AE is any untoward medical occurrence in a subjects participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Safety analysis set included all the subjects who were randomized and received at least one administration of study agent in the study.	
End point type	Secondary
End point timeframe:	
Up to Week 52 and up to Week 76	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Up to Week 52	77.9	80.1		
Up to Week 76	80.0	81.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Infections

End point title	Percentage of Subjects with Infections
End point description:	
Percentage of subjects with infections were reported. Safety analysis set included all the subjects who	

were randomized and received at least one administration of study agent in the study.

End point type	Secondary
End point timeframe:	
Up to Week 52 and up to Week 76	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Up to Week 52	40.5	34.0		
Up to Week 76	43.1	37.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Serious Infections

End point title	Percentage of Subjects with Serious Infections
End point description:	
Percentage of subjects with serious infections were reported. Safety analysis set included all the subjects who were randomized and received at least one administration of study agent in the study.	
End point type	Secondary
End point timeframe:	
Up to Week 52 and up to Week 76	

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Up to Week 52	2.6	2.1		
Up to Week 76	3.1	3.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Serious Adverse Events (SAEs)

End point title	Percentage of Subjects with Serious Adverse Events (SAEs)
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End point description:

Percentage of subjects with SAEs were reported. A SAE is any AE that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subjects and/or may require medical or surgical intervention to prevent one of the outcomes listed above. Coronavirus disease 2019 (COVID-19) related serious adverse events are adverse events with any of the following preferred terms "COVID-19", "Asymptomatic COVID-19", "Suspected COVID-19", "COVID-19 pneumonia", "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test positive" or with a reported term containing the string "COVI". Safety analysis set included all the subjects who were randomized and received at least one administration of study agent in the study.

End point type	Secondary
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End point timeframe:

Up to Week 52 and up to Week 76

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	191		
Units: percentage of subjects				
number (not applicable)				
Up to Week 52	16.4	13.1		
Up to Week 52: COVID-19 related SAEs	0	0		
Up to Week 76	19.5	15.2		
Up to Week 76: COVID-19 related SAEs	0	0.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Anti-drug Antibodies

End point title	Percentage of Subjects with Anti-drug Antibodies
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End point description:

Percentage of subjects with anti-drug antibodies were reported. Serum samples were assessed for anti-drug antibodies. Anti-drug assays were performed for ustekinumab and adalimumab. Immunogenicity analysis set included all subjects who had received at least 1 administration of study agent and have at least one valid blood sample drawn for detection of antibodies to study agent.

End point type	Secondary
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End point timeframe:

Up to Week 52

End point values	Adalimumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	190		
Units: percentage of subjects				
number (not applicable)	74.4	2.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 76

Adverse event reporting additional description:

Safety analysis set included all the subjects who were randomized and received at least one administration of study agent in the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Adalimumab
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Reporting group description:

Subjects received intravenous (IV) infusion of placebo for ustekinumab and 4 subcutaneous (SC) injections of adalimumab (each 40 milligrams [mg], total dose 160 mg) at Week 0, followed by 2 SC injections of adalimumab (each 40 mg, total dose 80 mg) at Week 2. From Week 4 to Week 56, subjects self-administered 1 SC injection of adalimumab 40 mg every 2 weeks (q2w).

Reporting group title	Ustekinumab
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Reporting group description:

Subjects received IV infusion of ustekinumab (approximately 6 milligram/kilogram [mg/kg]) and 4 SC injections of placebo for adalimumab at Week 0, followed by 2 SC injections of placebo at Week 2. From Week 4 to Week 56, subjects self-administered one SC injection of ustekinumab 90 mg every 8 weeks (q8w) starting at Week 8 and placebo adalimumab at the other designated q2w dosing intervals.

Serious adverse events	Adalimumab	Ustekinumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 195 (19.49%)	29 / 191 (15.18%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Vascular disorders			
Peripheral Vascular Disorder			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-Cardiac Chest Pain			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Death			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic Disorder			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Crush Injury			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic Vertebral Fracture			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Venolymphatic Malformation			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina Unstable			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness Postural			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Fistula			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Crohn's Disease			
subjects affected / exposed	17 / 195 (8.72%)	5 / 191 (2.62%)	
occurrences causally related to treatment / all	0 / 18	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Stenosis			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal Stenosis			
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Perforation			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Stenosis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestinal Obstruction			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			

subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile Duct Stone			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Chronic			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Foot Deformity			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Abscess			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Infection			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paracoccidioides Infection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Tuberculosis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Abscess			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Adalimumab	Ustekinumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	151 / 195 (77.44%)	152 / 191 (79.58%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Colon Adenoma			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Benign Neoplasm of Eye			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Seborrhoeic Keratosis			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Dysplastic Naevus			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Vascular disorders			
Aortic Arteriosclerosis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Deep Vein Thrombosis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	5 / 195 (2.56%)	3 / 191 (1.57%)	
occurrences (all)	5	3	
Hot Flush			

subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Raynaud's Phenomenon subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Surgical and medical procedures Tonsillectomy subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	1 / 191 (0.52%) 1	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Chest Discomfort subjects affected / exposed occurrences (all)	2 / 195 (1.03%) 2	0 / 191 (0.00%) 0	
Chest Pain subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	2 / 191 (1.05%) 2	
Drug Intolerance subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Fatigue subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	8 / 191 (4.19%) 10	
Impaired Healing subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	0 / 191 (0.00%) 0	
Injection Site Erythema subjects affected / exposed occurrences (all)	13 / 195 (6.67%) 65	3 / 191 (1.57%) 11	
Injection Site Bruising			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Influenza Like Illness		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Injection Site Haematoma		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Injection Site Irritation		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Injection Site Oedema		
subjects affected / exposed	3 / 195 (1.54%)	0 / 191 (0.00%)
occurrences (all)	6	0
Injection Site Pain		
subjects affected / exposed	3 / 195 (1.54%)	1 / 191 (0.52%)
occurrences (all)	14	1
Injection Site Reaction		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Injection Site Rash		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	3	1
Injection Site Pruritus		
subjects affected / exposed	7 / 195 (3.59%)	2 / 191 (1.05%)
occurrences (all)	28	10
Malaise		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Medical Device Pain		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Injection Site Swelling		
subjects affected / exposed	4 / 195 (2.05%)	0 / 191 (0.00%)
occurrences (all)	7	0
Oedema Peripheral		

subjects affected / exposed	0 / 195 (0.00%)	5 / 191 (2.62%)	
occurrences (all)	0	6	
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences (all)	2	1	
Peripheral Swelling			
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)	
occurrences (all)	2	2	
Pyrexia			
subjects affected / exposed	8 / 195 (4.10%)	6 / 191 (3.14%)	
occurrences (all)	10	7	
Suprapubic Pain			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Vessel Puncture Site Haematoma			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Drug Hypersensitivity			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Amenorrhoea			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Cervical Dysplasia			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Dysmenorrhoea			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Semen Discolouration			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Ovarian Cyst			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences (all)	2	1	
Nipple Pain			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Uterine Haemorrhage			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal Discomfort			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences (all)	2	1	
Asthma Late Onset			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Dyspnoea Exertional			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	2 / 195 (1.03%)	4 / 191 (2.09%)	
occurrences (all)	2	4	
Cough			

subjects affected / exposed	5 / 195 (2.56%)	3 / 191 (1.57%)	
occurrences (all)	6	3	
Bronchitis Chronic			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal Pain			
subjects affected / exposed	3 / 195 (1.54%)	9 / 191 (4.71%)	
occurrences (all)	3	11	
Nasal Crusting			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Nasal Congestion			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	2	
Rhinitis Allergic			
subjects affected / exposed	2 / 195 (1.03%)	3 / 191 (1.57%)	
occurrences (all)	4	3	
Pulmonary Embolism			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Pharyngeal Inflammation			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Respiratory Tract Congestion			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences (all)	2	1	
Psychiatric disorders			
Depressed Mood			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Affect Lability			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	

Anxiety			
subjects affected / exposed	3 / 195 (1.54%)	6 / 191 (3.14%)	
occurrences (all)	3	6	
Anxiety Disorder			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Sleep Disorder			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	2	
Panic Attack			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	4 / 195 (2.05%)	2 / 191 (1.05%)	
occurrences (all)	4	2	
Insomnia			
subjects affected / exposed	3 / 195 (1.54%)	1 / 191 (0.52%)	
occurrences (all)	3	1	
Stress			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Investigations			
Aspartate Aminotransferase Increased			
subjects affected / exposed	3 / 195 (1.54%)	3 / 191 (1.57%)	
occurrences (all)	3	3	
Alanine Aminotransferase Increased			
subjects affected / exposed	6 / 195 (3.08%)	2 / 191 (1.05%)	
occurrences (all)	7	2	
Blood Creatinine Increased			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Blood Folate Decreased			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Blood Phosphorus Increased			

subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Blood Glucose Increased		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Blood Pressure Increased		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Blood Testosterone Decreased		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Body Temperature Increased		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
C-Reactive Protein Increased		
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)
occurrences (all)	2	2
Colonoscopy Abnormal		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Faecal Calprotectin Increased		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Haematocrit Increased		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Heart Rate Increased		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Granulocyte Count Decreased		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Hepatic Enzyme Increased		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Human Chorionic Gonadotropin		

Increased			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Mycobacterium Tuberculosis Complex Test Positive			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Transaminases Increased			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Urine Output Increased			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Vitamin B12 Decreased			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Liver Function Test Increased			
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)	
occurrences (all)	2	2	
Weight Increased			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	2	
Weight Decreased			
subjects affected / exposed	3 / 195 (1.54%)	0 / 191 (0.00%)	
occurrences (all)	3	0	
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)	
occurrences (all)	1	2	
Exposure to Toxic Agent			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Fall		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Foreign Body in Eye		
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Hand Fracture		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Joint Injury		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Ligament Sprain		
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)
occurrences (all)	2	2
Muscle Strain		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3
Post Procedural Inflammation		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Procedural Anxiety		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Procedural Dizziness		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Procedural Pain		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Road Traffic Accident		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	2
Skin Laceration		

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Spinal Fracture			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Splinter			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Tibia Fracture			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Tooth Fracture			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Tooth Injury			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Syringomyelia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	2	
Extrasystoles			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Nervous system disorders			

Cervical Radiculopathy		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Amnesia		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Dysgeusia		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Headache		
subjects affected / exposed	14 / 195 (7.18%)	25 / 191 (13.09%)
occurrences (all)	25	40
Dizziness		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Dizziness Postural		
subjects affected / exposed	0 / 195 (0.00%)	4 / 191 (2.09%)
occurrences (all)	0	4
Hypoaesthesia		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	2	1
Lethargy		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Hemiplegic Migraine		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Migraine with Aura		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Migraine		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Nerve Compression		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2

Paraesthesia			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	2	
Memory Impairment			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Sinus Headache			
subjects affected / exposed	0 / 195 (0.00%)	4 / 191 (2.09%)	
occurrences (all)	0	4	
Presyncope			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)	
occurrences (all)	0	3	
Tremor			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	3	
Tension Headache			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Syncope			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	2	
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Anaemia			
subjects affected / exposed	7 / 195 (3.59%)	6 / 191 (3.14%)	
occurrences (all)	9	6	
Lymphadenopathy			

subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Lymphadenitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear Haemorrhage			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Ear Pain			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Ear Swelling			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Vertigo			
subjects affected / exposed	4 / 195 (2.05%)	7 / 191 (3.66%)	
occurrences (all)	4	7	
Eye disorders			
Blepharospasm			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Cataract			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Choroidal Effusion		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	2
Dry Eye		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Conjunctivitis Allergic		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Eye Pruritus		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Eyelid Oedema		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Eyelid Cyst		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Foreign Body Sensation in Eyes		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Iritis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Iridocyclitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Glaucoma		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Keratitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Uveitis		

subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Swelling of Eyelid subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Retinal Detachment subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 2	0 / 191 (0.00%) 0	
Vision Blurred subjects affected / exposed occurrences (all)	3 / 195 (1.54%) 3	1 / 191 (0.52%) 1	
Gastrointestinal disorders			
Abdominal Distension subjects affected / exposed occurrences (all)	2 / 195 (1.03%) 2	2 / 191 (1.05%) 2	
Abdominal Hernia subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Abdominal Pain subjects affected / exposed occurrences (all)	16 / 195 (8.21%) 20	25 / 191 (13.09%) 36	
Abdominal Pain Lower subjects affected / exposed occurrences (all)	2 / 195 (1.03%) 2	1 / 191 (0.52%) 1	
Abdominal Pain Upper subjects affected / exposed occurrences (all)	5 / 195 (2.56%) 6	7 / 191 (3.66%) 7	
Abdominal Tenderness subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Anal Fissure subjects affected / exposed occurrences (all)	2 / 195 (1.03%) 2	7 / 191 (3.66%) 7	
Anal Stenosis subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	

Anal Pruritus		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3
Anal Fistula		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Anorectal Discomfort		
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Chronic Gastritis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Crohn's Disease		
subjects affected / exposed	29 / 195 (14.87%)	20 / 191 (10.47%)
occurrences (all)	33	25
Constipation		
subjects affected / exposed	7 / 195 (3.59%)	7 / 191 (3.66%)
occurrences (all)	7	7
Defaecation Urgency		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Dental Caries		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Diarrhoea Haemorrhagic		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Diarrhoea		
subjects affected / exposed	2 / 195 (1.03%)	11 / 191 (5.76%)
occurrences (all)	2	11
Dyspepsia		
subjects affected / exposed	4 / 195 (2.05%)	4 / 191 (2.09%)
occurrences (all)	5	6
Eosinophilic Oesophagitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0

Enlarged Uvula		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	1 / 195 (0.51%)	4 / 191 (2.09%)
occurrences (all)	1	7
Food Poisoning		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Gastric Ulcer		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Frequent Bowel Movements		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Gastritis		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Gastritis Erosive		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Gastrooesophageal Reflux Disease		
subjects affected / exposed	5 / 195 (2.56%)	6 / 191 (3.14%)
occurrences (all)	5	6
Gingival Swelling		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Haematochezia		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3
Haemorrhoids		
subjects affected / exposed	1 / 195 (0.51%)	3 / 191 (1.57%)
occurrences (all)	1	3
Ileal Stenosis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1

Large Intestinal Stenosis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Mouth Ulceration		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Mouth Haemorrhage		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Lip Blister		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Rectal Haemorrhage		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3
Proctitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Nausea		
subjects affected / exposed	9 / 195 (4.62%)	12 / 191 (6.28%)
occurrences (all)	9	13
Rectal Tenesmus		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Small Intestinal Obstruction		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Stomatitis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Vomiting		
subjects affected / exposed	4 / 195 (2.05%)	11 / 191 (5.76%)
occurrences (all)	4	15
Toothache		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2

Subileus subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	0 / 191 (0.00%) 0	
Hepatobiliary disorders			
Cholangitis Sclerosing subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	0 / 191 (0.00%) 0	
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	0 / 191 (0.00%) 0	
Hepatic Steatosis subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	1 / 191 (0.52%) 1	
Cholecystitis subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Jaundice subjects affected / exposed occurrences (all)	1 / 195 (0.51%) 1	0 / 191 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	3 / 195 (1.54%) 3	2 / 191 (1.05%) 2	
Alopecia subjects affected / exposed occurrences (all)	3 / 195 (1.54%) 3	7 / 191 (3.66%) 7	
Brow Ptosis subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	1 / 191 (0.52%) 1	
Dermatitis subjects affected / exposed occurrences (all)	2 / 195 (1.03%) 2	1 / 191 (0.52%) 1	
Dermatitis Contact subjects affected / exposed occurrences (all)	0 / 195 (0.00%) 0	4 / 191 (2.09%) 5	
Drug Eruption			

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Dry Skin		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Eczema		
subjects affected / exposed	4 / 195 (2.05%)	4 / 191 (2.09%)
occurrences (all)	4	4
Eczema Nummular		
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Erythema Nodosum		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Erythema		
subjects affected / exposed	4 / 195 (2.05%)	0 / 191 (0.00%)
occurrences (all)	5	0
Hidradenitis		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Hyperhidrosis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Ingrowing Nail		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Night Sweats		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	2	1
Photosensitivity Reaction		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Petechiae		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Post Inflammatory Pigmentation		

Change		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Pseudofolliculitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Pruritus		
subjects affected / exposed	3 / 195 (1.54%)	2 / 191 (1.05%)
occurrences (all)	3	2
Psoriasis		
subjects affected / exposed	3 / 195 (1.54%)	2 / 191 (1.05%)
occurrences (all)	4	2
Rash		
subjects affected / exposed	6 / 195 (3.08%)	3 / 191 (1.57%)
occurrences (all)	6	3
Rash Erythematous		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Rash Papular		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Rash Pruritic		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	2	1
Rosacea		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Scar Pain		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Sebaceous Hyperplasia		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Seborrhoeic Dermatitis		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1

Skin Exfoliation			
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)	
occurrences (all)	2	1	
Skin Fissures			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Skin Lesion			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Vitiligo			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)	
occurrences (all)	2	2	
Skin Ulcer			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Chronic Kidney Disease			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Haematuria			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Dysuria			

subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Ankylosing Spondylitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	15 / 195 (7.69%)	13 / 191 (6.81%)	
occurrences (all)	19	19	
Back Pain			
subjects affected / exposed	4 / 195 (2.05%)	8 / 191 (4.19%)	
occurrences (all)	4	9	
Arthritis Enteropathic			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Bone Pain			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Arthritis			
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Fistula			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Fibromyalgia			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Diastasis Recti Abdominis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Flank Pain			

subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Lupus-Like Syndrome		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Muscle Spasms		
subjects affected / exposed	3 / 195 (1.54%)	2 / 191 (1.05%)
occurrences (all)	3	2
Musculoskeletal Chest Pain		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Joint Swelling		
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Osteopenia		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Musculoskeletal Pain		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Neck Pain		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Plantar Fasciitis		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Pain in Extremity		
subjects affected / exposed	1 / 195 (0.51%)	3 / 191 (1.57%)
occurrences (all)	1	3
Periarthritis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Pathological Fracture		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Sacroiliitis		

subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Psoriatic Arthropathy			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
SAPHO Syndrome			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Synovial Cyst			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Temporomandibular Joint Syndrome			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Spinal Pain			
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)	
occurrences (all)	0	3	
Tenosynovitis Stenosans			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)	
occurrences (all)	0	2	
Abscess Limb			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Acute Sinusitis			
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)	
occurrences (all)	2	0	
Abscess Oral			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	

Anal Abscess		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	2
Asymptomatic COVID-19		
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)
occurrences (all)	2	2
Bacterial Vulvovaginitis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Blister Infected		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Bronchitis		
subjects affected / exposed	3 / 195 (1.54%)	0 / 191 (0.00%)
occurrences (all)	3	0
COVID-19		
subjects affected / exposed	4 / 195 (2.05%)	1 / 191 (0.52%)
occurrences (all)	4	1
Bronchitis Bacterial		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Candida Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Conjunctivitis		
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Cervicitis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Cellulitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Cystitis		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3

Dermatophytosis of Nail		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Ear Infection		
subjects affected / exposed	1 / 195 (0.51%)	3 / 191 (1.57%)
occurrences (all)	1	3
Eye Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Eczema Infected		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Folliculitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Furuncle		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	3
Fungal Skin Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Gastroenteritis		
subjects affected / exposed	3 / 195 (1.54%)	3 / 191 (1.57%)
occurrences (all)	3	4
Gastroenteritis Viral		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Hepatitis E		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Genital Herpes		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Gastrointestinal Viral Infection		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1

Gastrointestinal Bacterial Overgrowth		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Laryngitis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	5 / 195 (2.56%)	6 / 191 (3.14%)
occurrences (all)	5	6
Herpes Zoster Disseminated		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Large Intestine Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Herpes Zoster		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	2	1
Latent Tuberculosis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Localised Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	20 / 195 (10.26%)	14 / 191 (7.33%)
occurrences (all)	22	17
Lower Respiratory Tract Infection		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	2	1
Oral Herpes		
subjects affected / exposed	11 / 195 (5.64%)	1 / 191 (0.52%)
occurrences (all)	13	1
Oral Candidiasis		

subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Onychomycosis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Oropharyngeal Candidiasis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Otitis Externa		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Otitis Media		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Pharyngitis		
subjects affected / exposed	2 / 195 (1.03%)	1 / 191 (0.52%)
occurrences (all)	2	1
Pharyngitis Streptococcal		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	2
Pneumonia		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Post Procedural Infection		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Postoperative Wound Infection		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Respiratory Syncytial Virus Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Rectal Abscess		
subjects affected / exposed	0 / 195 (0.00%)	2 / 191 (1.05%)
occurrences (all)	0	2
Respiratory Tract Infection		

subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Respiratory Tract Infection Viral		
subjects affected / exposed	3 / 195 (1.54%)	1 / 191 (0.52%)
occurrences (all)	3	1
Salmonellosis		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Rhinitis		
subjects affected / exposed	3 / 195 (1.54%)	2 / 191 (1.05%)
occurrences (all)	3	3
Septic Shock		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Sinobronchitis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Streptococcal Infection		
subjects affected / exposed	2 / 195 (1.03%)	0 / 191 (0.00%)
occurrences (all)	2	0
Staphylococcal Skin Infection		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Sinusitis		
subjects affected / exposed	7 / 195 (3.59%)	3 / 191 (1.57%)
occurrences (all)	8	3
Suspected COVID-19		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Tonsillitis		
subjects affected / exposed	3 / 195 (1.54%)	3 / 191 (1.57%)
occurrences (all)	4	3
Tooth Abscess		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3
Tooth Infection		

subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)	
occurrences (all)	1	2	
Tracheobronchitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	15 / 195 (7.69%)	13 / 191 (6.81%)	
occurrences (all)	16	16	
Vaginal Infection			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	2	
Urinary Tract Infection			
subjects affected / exposed	11 / 195 (5.64%)	7 / 191 (3.66%)	
occurrences (all)	12	13	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 195 (1.03%)	2 / 191 (1.05%)	
occurrences (all)	2	2	
Viral Infection			
subjects affected / exposed	4 / 195 (2.05%)	3 / 191 (1.57%)	
occurrences (all)	4	3	
Vulvitis			
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)	
occurrences (all)	0	1	
Vulvovaginal Candidiasis			
subjects affected / exposed	1 / 195 (0.51%)	4 / 191 (2.09%)	
occurrences (all)	1	5	
Vulvovaginal Mycotic Infection			
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)	
occurrences (all)	1	0	
Decreased Appetite			

subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Hypoferritinaemia		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Hypercholesterolaemia		
subjects affected / exposed	1 / 195 (0.51%)	2 / 191 (1.05%)
occurrences (all)	1	2
Hypercalcaemia		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Hypokalaemia		
subjects affected / exposed	1 / 195 (0.51%)	0 / 191 (0.00%)
occurrences (all)	1	0
Folate Deficiency		
subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)
occurrences (all)	1	1
Iron Deficiency		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Impaired Fasting Glucose		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Hypovitaminosis		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	1
Hypophosphataemia		
subjects affected / exposed	0 / 195 (0.00%)	1 / 191 (0.52%)
occurrences (all)	0	2
Vitamin D Deficiency		
subjects affected / exposed	1 / 195 (0.51%)	5 / 191 (2.62%)
occurrences (all)	1	5
Vitamin B12 Deficiency		
subjects affected / exposed	0 / 195 (0.00%)	3 / 191 (1.57%)
occurrences (all)	0	3
Type 2 Diabetes Mellitus		

subjects affected / exposed	1 / 195 (0.51%)	1 / 191 (0.52%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2019	The overall reason of the amendment was to clarify the definition of endoscopic remission, to update the tuberculosis test being used; to add instructions for emergency un-blinding; and add a few clarifications.
14 December 2020	The overall reason of the amendment was to revise or clarify secondary, other, and patient-reported outcome (PRO) endpoints for this study, adding Type 1 error control for major secondary endpoints, updating several secondary endpoints, adding or revising several PRO endpoints, and clarifying the wording of some endpoints. The added endpoints were to better address subject concerns regarding treatment of Crohn's disease, and health authority interest pertaining to efficacy. With this amendment, the updated revisions to the study endpoints were pre-specified prior to database lock.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported