Clinical trial results:
Study of Treat to Target Versus Routine Care Maintenance Strategies in Crohn's Disease Patients Treated with Ustekinumab

Summary

EudraCT number	2016-002918-43
Trial protocol	GB SE ES BE DE NL FR PT SK DK IT
Global end of trial date	20 July 2021

Results information

Result version number	v1 (current)
This version publication date	30 July 2022
First version publication date	30 July 2022

Trial information

Trial identification

Sponsor protocol code	CNTO1275CRD3005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03107793
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V., 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	20 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the efficacy of a Treat to Target (T2T) strategy coupled with early endoscopic assessment versus a clinically driven (routine care [RC]) approach in achieving endoscopic response.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 29
Country: Number of subjects enrolled	Czechia: 24
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Italy: 166
Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	Portugal: 37
Country: Number of subjects enrolled	Slovakia: 30
Country: Number of subjects enrolled	Spain: 47
Country: Number of subjects enrolled	Sweden: 15
Country: Number of subjects enrolled	United Kingdom: 39
Worldwide total number of subjects	498
EEA total number of subjects	459

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)	485
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 500 enrolled subjects who received at least 1 dose of study medication, 498 subjects were included in the analysis because study team decided to exclude one site due to compliance issue. Hence, number of subjects who received at least one dose of study medication reduced from 500 to 498 subjects.

Period 1

Period 1 title	Induction Period (16 Weeks)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Induction Period: Ustekinumab (6 Milligrams [mg]/Kilogram[kg])

Arm description:

Subjects were administered with approximately 6 mg/kg intravenous (IV) injection of ustekinumab at Week 0 and 90 mg subcutaneous (SC) injection of ustekinumab at Week 8. At Week 16, subjects who did not achieve a Crohn's Disease Activity Index (CDAI) improvement (non-responders) of greater than or equal to (>=) 70 points versus Week 0 (CDAI-70), left the study. Subjects who achieved CDAI improvement (responders) of at least 70 points versus Week 0 were randomised in open-label maintenance period either with treat to target arm or routine care arm.

Arm type	Experimental
Investigational medicinal product name	Ustekinumab 90 mg
Investigational medicinal product code	
Other name	STELARA
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 90 mg was administered through SC injection at Week 8.

Investigational medicinal product name	Ustekinumab 6 mg/kg
Investigational medicinal product code	
Other name	STELARA
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ustekinumab 6 mg/kg was administered through IV injection at Week 0.

Number of subjects in period 1	Induction Period: Ustekinumab (6 Milligrams [mg]/Kilogram[kg])
Started	498
Completed	488
Not completed	10
Consent withdrawn by subject	3

Physician decision	1
Adverse event	5
Progressive disease	1

Period 2

Period 2 title	Maintenance Period (Week 16-Week 48)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treat to Target

Arm description:

Subjects with less than (<) 25 percent (%) improvement in simple endoscopic score for Crohn's disease (SES-CD) at Week 16 versus baseline received ustekinumab 90 mg SC dose 8-weekly maintenance treatment while subjects with >= 25% improvement in SES-CD score at Week 16 versus baseline received ustekinumab 90 mg SC dose 12-weekly treatment based on centrally-read ileocolonoscopy findings. From Week 24 for subjects assigned to the 8-weekly regimen or from Week 20 for the 12-weekly regimen group ustekinumab 90 mg SC maintenance treatment was directed by treat to target assessments based on C-reactive protein (CRP) and CDAI assessments. Subjects previously on 12-weekly regimens were adjusted to 8-weekly dosing; those previously on 8-weekly regimens were adjusted to 4-weekly dosing. Subjects subsequently failing to meet treatment targets at the next assessment visit 4 weeks after dosing were not able to optimize dosing further and left the study.

Arm type	Experimental
Investigational medicinal product name	Ustekinumab 90 mg
Investigational medicinal product code	
Other name	STELARA
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 90 mg was administered through SC injection.

Arm title	Routine Care

Arm description:

Subjects received ustekinumab 90 mg SC dose every 8-weeks or every 12-weeks according to clinical judgment. At Week 16, (that is, 8 weeks after the first SC dose), subjects who did not show adequate response based on the investigator's judgment received a second ustekinumab 90 mg SC dose at that time. Clinical assessments in case of disease flare were performed at investigator's discretion. Subjects who lost response during 12-weekly could adjust the dosing to 8-weekly maintenance treatment. Subjects previously received 8-weekly ustekinumab treatment were unable to adjust the dose following disease flare and left the study as per investigator's judgment.

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab 90 mg
Investigational medicinal product code	
Other name	STELARA
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 90 mg was administered through SC injection.

Number of subjects in period 2[1]	Treat to Target	Routine Care
Started	219	221
Completed	173	193
Not completed	46	28
Consent withdrawn by subject	12	4
Physician decision	1	2
Received a disallowed concomitant treatment	-	1
Death	2	-
Disease relapse	2	1
Pregnancy	1	1
Adverse event	6	10
Lost to follow-up	1	-
Progressive disease	-	1
Lack of efficacy	21	8

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of 488 subjects who completed the induction period, 48 subjects were not randomized in Maintenance period due to reasons such as, non CDAI-70 responders at Week 16, lack of Efficacy, adverse events, pregnancy, withdrawal by subjects, etc.

Period 3

Period 3 title	Extension Period (Week 48-Week 104)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treat to Target

Arm description:

From Week 48, subjects continued to receive SC ustekinumab 90 mg in the long-term extension (LTE) period up to Week 104. The frequency of ustekinumab dosing with escalation/de-escalation between once in 12 weeks (q12w)/q8w/q4w was based on the following targets: endoscopic remission (CD [SES-CD] score less than or equal to [<=] 2) and corticosteroid (CS)-free clinical remission (CDAI score of <150 points of >=16 weeks duration) at Week 48; and later, on CS-free clinical remission and biomarker remission (C-reactive protein <=10 miligrams per liter [mg/L] and fecal calprotectin <=250 micrograms per gram [mcg/g]) at 2 consecutive visits 8 weeks apart. Subjects on q4w dosing failing to reach targets were discontinued.

Arm type	Experimental

Investigational medicinal product name	Ustekinumab 90 mg
Investigational medicinal product code	
Other name	STELARA
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 90 mg was administered through SC injection.

Arm title	Routine Care

Arm description:

From Week 48, subjects continued to receive SC ustekinumab 90 mg in the long-term extension (LTE) period up to Week 104. The frequency of ustekinumab dosing with escalation/de-escalation between once in 12 weeks (q12w)/q8w/q4w was based on the following targets: endoscopic remission (CD [SES-CD] score <=2) and corticosteroid (CS)-free clinical remission (CDAI score of <150 points of >=16 weeks duration) at Week 48; and later, on CS-free clinical remission and biomarker remission (C-reactive protein <=10 mg/L and fecal calprotectin <=250 mcg/g) at 2 consecutive visits 8 weeks apart. Subjects on q4w dosing failing to reach targets were discontinued.

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab 90 mg
Investigational medicinal product code	
Other name	STELARA
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab 90 mg was administered through SC injection.

Number of subjects in period 3[2]	Treat to Target	Routine Care
Started	147	176
Completed	119	139
Not completed	28	37
Consent withdrawn by subject	5	9
Physician decision	-	2
Did not re-consent to protocol amendment 3	-	1
Death	-	1
Pregnancy	2	4
Disease relapse	-	3
Adverse event	10	3
Non-compliance with study drug	1	-
Unspecified	1	3
Lost to follow-up	1	2
Lack of efficacy	8	9

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of 366 subjects who completed the maintenance period, 43 subjects were not randomized in Extension period.

Baseline characteristics

Reporting groups	
Reporting group title	Induction Period: Ustekinumab (6 Milligrams [mg]/Kilogram[kg])

Reporting group description:

Subjects were administered with approximately 6 mg/kg intravenous (IV) injection of ustekinumab at Week 0 and 90 mg subcutaneous (SC) injection of ustekinumab at Week 8. At Week 16, subjects who did not achieve a Crohn's Disease Activity Index (CDAI) improvement (non-responders) of greater than or equal to (>=) 70 points versus Week 0 (CDAI-70), left the study. Subjects who achieved CDAI improvement (responders) of at least 70 points versus Week 0 were randomised in open-label maintenance period either with treat to target arm or routine care arm.

Reporting group values	Induction Period: Ustekinumab (6 Milligrams [mg]/Kilogram[kg])	Total	
Number of subjects	498	498	
Title for AgeCategorical Units: subjects			
children	0	0	
adolescents	0	0	
adults	485	485	
elderly 65 to 84	13	13	
elderly over 85	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	37		
standard deviation	± 12.96	-	
Title for Gender Units: subjects			
Female	257	257	
Male	241	241	

End points

End points reporting groups

Reporting group title	Induction Period: Ustekinumab (6 Milligrams [mg]/Kilogram[kg])

Reporting group description:

Subjects were administered with approximately 6 mg/kg intravenous (IV) injection of ustekinumab at Week 0 and 90 mg subcutaneous (SC) injection of ustekinumab at Week 8. At Week 16, subjects who did not achieve a Crohn's Disease Activity Index (CDAI) improvement (non-responders) of greater than or equal to (>=) 70 points versus Week 0 (CDAI-70), left the study. Subjects who achieved CDAI improvement (responders) of at least 70 points versus Week 0 were randomised in open-label maintenance period either with treat to target arm or routine care arm.

Reporting group title	Treat to Target

Reporting group description:

Subjects with less than (<) 25 percent (%) improvement in simple endoscopic score for Crohn's disease (SES-CD) at Week 16 versus baseline received ustekinumab 90 mg SC dose 8-weekly maintenance treatment while subjects with >= 25% improvement in SES-CD score at Week 16 versus baseline received ustekinumab 90 mg SC dose 12-weekly treatment based on centrally-read ileocolonoscopy findings. From Week 24 for subjects assigned to the 8-weekly regimen or from Week 20 for the 12-weekly regimen group ustekinumab 90 mg SC maintenance treatment was directed by treat to target assessments based on C-reactive protein (CRP) and CDAI assessments. Subjects previously on 12-weekly regimens were adjusted to 8-weekly dosing; those previously on 8-weekly regimens were adjusted to 4-weekly dosing. Subjects subsequently failing to meet treatment targets at the next assessment visit 4 weeks after dosing were not able to optimize dosing further and left the study.

Reporting group title	Routine Care

Reporting group description:

Subjects received ustekinumab 90 mg SC dose every 8-weeks or every 12-weeks according to clinical judgment. At Week 16, (that is, 8 weeks after the first SC dose), subjects who did not show adequate response based on the investigator's judgment received a second ustekinumab 90 mg SC dose at that time. Clinical assessments in case of disease flare were performed at investigator's discretion. Subjects who lost response during 12-weekly could adjust the dosing to 8-weekly maintenance treatment. Subjects previously received 8-weekly ustekinumab treatment were unable to adjust the dose following disease flare and left the study as per investigator's judgment.

Reporting group title	Treat to Target

Reporting group description:

From Week 48, subjects continued to receive SC ustekinumab 90 mg in the long-term extension (LTE) period up to Week 104. The frequency of ustekinumab dosing with escalation/de-escalation between once in 12 weeks (q12w)/q8w/q4w was based on the following targets: endoscopic remission (CD [SES-CD] score less than or equal to [<=] 2) and corticosteroid (CS)-free clinical remission (CDAI score of <150 points of >=16 weeks duration) at Week 48; and later, on CS-free clinical remission and biomarker remission (C-reactive protein <=10 miligrams per liter [mg/L] and fecal calprotectin <=250 micrograms per gram [mcg/g]) at 2 consecutive visits 8 weeks apart. Subjects on q4w dosing failing to reach targets were discontinued.

Reporting group title	Routine Care

Reporting group description:

From Week 48, subjects continued to receive SC ustekinumab 90 mg in the long-term extension (LTE) period up to Week 104. The frequency of ustekinumab dosing with escalation/de-escalation between once in 12 weeks (q12w)/q8w/q4w was based on the following targets: endoscopic remission (CD [SES-CD] score <=2) and corticosteroid (CS)-free clinical remission (CDAI score of <150 points of >=16 weeks duration) at Week 48; and later, on CS-free clinical remission and biomarker remission (C-reactive protein <=10 mg/L and fecal calprotectin <=250 mcg/g) at 2 consecutive visits 8 weeks apart. Subjects on q4w dosing failing to reach targets were discontinued.

Primary: Percentage of Subjects With Endoscopic Response at Week 48

End point title	Percentage of Subjects With Endoscopic Response at Week 48

End point description:

Endoscopic response defined as showing a reduction from baseline in simple endoscopic score for Crohn's disease (SES-CD) of >=50%. SES-CD is a validated instrument reflecting an endoscopist global

appraisal of mucosal lesions in Crohn's disease. SES-CD grades lesions by location (5 bowel segments: ileum, right colon, transverse colon, left colon, and rectum) using 4 endoscopic variables: ulcer size, extent of ulcerated surface, extent of affected surface, and presence/type of narrowing. Total SES-CD is sum of 4 variables for all 5 bowel segments. Scores range from 0-60 with higher scores indicating more severe disease. Randomised subjects who stopped treatment before reaching Week 48 due to any reason, or subjects without endoscopic data at Week 48 were considered as nonresponders. Full randomised analysis set (FRAS) included all subjects who received at least 1 dose of study agent and were randomised at Week 16, regardless of study treatment being administered once randomised.

End point type	Primary

End point timeframe:

Week 48

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)	37.9 (31.4 to 44.7)	29.9 (23.9 to 36.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Treat to Target v Routine Care
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0871
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Subjects With Endoscopic Response at Week 48 (Premature Drop-outs Excluded)

End point title	Percentage of Subjects With Endoscopic Response at Week 48 (Premature Drop-outs Excluded)

End point description:

Endoscopic response defined as showing a reduction from baseline in SES-CD (a validated instrument reflecting an endoscopist's global appraisal of mucosal lesions) score of >=50%. SES-CD grades lesions by location (5 bowel segments: ileum, right colon, transverse colon, left colon, and rectum) using 4 endoscopic variables: ulcer size, extent of ulcerated surface, extent of affected surface, and presence/type of narrowing. Total SES-CD is calculated as sum of 4 variables for 5 bowel segments. Scores ranges 0-60. Higher scores indicates more severe disease. Randomised subjects who stopped treatment before reaching Week 48 due to reasons other than lack/loss of efficacy were excluded from analysis. FRAS included all subjects who received at least 1 dose of study agent and were randomised at Week 16, regardless of study treatment being administered once randomised. Here, 'N' (Number analysed) included subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 48

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	198		
Units: Percentage of Subjects				
number (confidence interval 95%)	43.0 (35.9 to 50.3)	32.3 (25.9 to 39.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Endoscopic Response at Week 48 (Last Observation Carried Forward [LOCF])

End point title	Percentage of Subjects With Endoscopic Response at Week 48 (Last Observation Carried Forward [LOCF])

End point description:

Endoscopic response defined as a reduction from baseline in SES-CD score of >= 50%. SES-CD is a validated instrument reflecting an endoscopist global appraisal of mucosal lesions in Crohn's disease. SES-CD grades lesions by location (5 bowel segments: ileum, right colon, transverse colon, left colon, and rectum) using 4 endoscopic variables: ulcer size, extent of ulcerated surface, extent of affected surface, and presence/type of narrowing. The total SES-CD was calculated as the sum of the 4 variables for the 5 bowel segments. Scores range from 0 to 60, with higher scores indicating more severe disease. Last observation carried forward: subjects who had a missing SES-CD score at Week 48 or who stopped treatment before reaching Week 48 had their last SES-CD score carried forward. FRAS included subjects who received at least 1 dose of study agent and were randomised at Week 16, regardless of study treatment being administered once randomised.

End point type	Secondary

End point timeframe:

Week 48

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)	40.2 (33.6 to 47.0)	30.8 (24.8 to 37.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Response at Weeks 16, 48, and Endpoint (LOCF)

End point title	Percentage of Subjects With Clinical Response at Weeks 16, 48, and Endpoint (LOCF)

End point description:

Clinical response defined as a >=100-point reduction from the baseline in Crohn's Disease Activity Index (CDAI) score, or a CDAI score of <150. 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. In general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. Subjects with missing data were analyzed as non-responder. FRAS included all subjects who received at least 1 dose of study agent and were randomised at Week 16, regardless of study treatment being administered once randomised. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (that is, first 48 weeks of the study).

End point type	Secondary

End point timeframe:

Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16	85.4 (80.0 to 89.8)	89.6 (84.8 to 93.3)		
Week 48	68.0 (61.4 to 74.2)	77.8 (71.8 to 83.1)		
Endpoint (LOCF)	89.5 (84.7 to 93.2)	89.6 (84.8 to 93.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Remission at Weeks 16, 48, and Endpoint (LOCF)

End point title	Percentage of Subjects With Clinical Remission at Weeks 16, 48, and Endpoint (LOCF)

End point description:

Clinical Remission defined as a CDAI score of <150 points. 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. In general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. Subjects with missing data were analysed as non-remitter. FRAS included all subjects who received at least 1 dose of study agent and were randomised at Week 16, regardless of study treatment being administered once randomised. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (that is, first 48 weeks of the study).

End point type	Secondary

End point timeframe:

Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16	72.1 (65.7 to 78.0)	74.2 (67.9 to 79.8)		
Week 48	61.6 (54.9 to 68.1)	69.7 (63.2 to 75.7)		
Endpoint (LOCF)	77.2 (71.0 to 82.6)	78.3 (72.3 to 83.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Endoscopic Remission at Weeks 16, 48, and Endpoint (LOCF)

End point title	Percentage of Subjects With Endoscopic Remission at Weeks 16, 48, and Endpoint (LOCF)

End point description:

Endoscopic remission defined as SES-CD <=2. SES-CD is a validated instrument reflecting an endoscopist global appraisal of mucosal lesions in Crohn's disease. It grades lesions by location: 5 bowel segments: ileum,right colon, transverse colon, left colon and rectum, using 4 endoscopic variables: ulcer size,extent of ulcerated surface,extent of affected surface,and presence/type of narrowing. Total score is sum of 4 variables. Scores range 0-60. Higher scores means severe disease. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e, first 48 weeks). FRAS was used. Here, 'n' (number analysed) refers subjects analysed at specified timepoints. '99999' refers to data not collected for routine care arm at Week 16 as per planned analysis.

End point type	Secondary

End point timeframe:

Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16 (n=219, 0)	11.4 (7.5 to 16.4)	99999 (99999 to 99999)		
Week 48 (n=219, 221)	11.4 (7.5 to 16.4)	14.5 (10.1 to 19.8)		
Endpoint (LOCF) (n=219, 221)	11.9 (7.9 to 16.9)	15.4 (10.9 to 20.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Mucosal Healing at Weeks 16, 48, and Endpoint (LOCF)

End point title	Percentage of Subjects With Mucosal Healing at Weeks 16, 48, and Endpoint (LOCF)

End point description:

Mucosal healing defined as complete absence of mucosal ulcerations in any ileocolonic segment. SES-CD is a validated instrument reflecting an endoscopist global appraisal of mucosal lesions in Crohn's disease. It grades lesions by location: 5 bowel segments: ileum, right colon, transverse colon, left colon, and rectum, using 4 endoscopic variables: ulcer size,extent of ulcerated surface,extent of affected surface,and presence/type of narrowing. Total score is sum of 4 variables. Scores range 0-60. Higher scores means severe disease. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. FRAS was used. Endpoint defined as last available postbaseline result within main analysis period (i.e, first 48 weeks). Here, 'n' (number analysed) included subjects analysed at specified timepoints. '99999' refers to data was not collected for routine care arm at Week 16 as per planned analysis.

End point type	Secondary

End point timeframe:

Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16 (n=219, 0)	16.0 (11.4 to 21.5)	99999 (99999 to 99999)		
Week 48 (n=219,221)	14.2 (9.8 to 19.5)	16.7 (12.1 to 22.3)		
Endpoint (LOCF) (n=219, 221)	14.6 (10.2 to 20.0)	17.6 (12.9 to 23.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Corticosteroid-free Clinical Remission at Week 48 and Endpoint (LOCF)

End point title	Percentage of Subjects With Corticosteroid-free Clinical Remission at Week 48 and Endpoint (LOCF)

End point description:

Corticosteroid-free Clinical Remission at Week 48 and Endpoint (LOCF) is defined as a CDAI score < 150 and not taking any corticosteroids for at least 30 days prior to Week 48 and Endpoint assessment. 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. In general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. Subjects with missing data were analysed as non-remitter. LOCF: subjects who had a missing SES-CD score at Week 48 or who stopped treatment before reaching Week 48 had their last SES-CD score carried forward. FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks of the study).

End point type	Secondary
End point timeframe: Week 48 and Endpoint (LOCF)	

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 48	56.6 (49.8 to 63.3)	63.3 (56.6 to 69.7)		
Endpoint (LOCF)	70.8 (64.3 to 76.7)	69.7 (63.2 to 75.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Corticosteroid-free Endoscopic Response at Week 16, 48, and Endpoint (LOCF)

End point title	Percentage of Subjects With Corticosteroid-free Endoscopic Response at Week 16, 48, and Endpoint (LOCF)

End point description:

Corticosteroid-free endoscopic response defined as a reduction from baseline in SES-CD score of >=50% and not taking any corticosteroids for at least 30 days prior to Weeks 16, 48, and endpoint. SES-CD is validated instrument reflecting an endoscopist global appraisal of mucosal lesions in Crohn's disease. It grades lesions by location: 5 bowel segments: ileum,right colon,transverse colon,left colon, and rectum, using 4 endoscopic variables: ulcer size, extent of ulcerated surface, extent of affected surface, and presence/type of narrowing.Total score is sum of 4 variables. Scores range 0-60. Higher scores means severe disease. LOCF:subjects who had missing score or stopped treatment before Week 48 had last score carried forward. FRAS was used. Endpoint defined as last available postbaseline result within main analysis period (i.e, first 48 weeks).Here 'n' (number analysed) refers subjects analysed at specified timepoints. '99999' refers to data not collected as per planned analysis.

End point type	Secondary
End point timeframe: Week 16, 48, and Endpoint (LOCF)	

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16 (n=219, 0)	26.5 (20.8 to 32.9)	99999 (99999 to 99999)		
Week 48 (n=219, 221)	33.8 (27.6 to 40.5)	28.5 (22.7 to 34.9)		

Endpoint (LOCF) (n=219, 221)	36.1 (29.7 to 42.8)	29.4 (23.5 to 35.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum C-reactive Protein (CRP)

End point title	Change from Baseline in Serum C-reactive Protein (CRP)

End point description:

Change from baseline in serum CRP were reported. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (that is, first 48 weeks of the study). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. Here, 'N' (Number analysed) included subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	218	219		
Units: Milligrams per litre (mg/L)				
arithmetic mean (standard deviation)				
Change at Week 16	-7.717 (± 22.0246)	-7.345 (± 17.5658)		
Change at Week 48	-7.839 (± 22.6777)	-7.909 (± 22.2139)		
Change at Endpoint (LOCF)	-7.839 (± 22.6777)	-7.909 (± 22.2139)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fecal Calprotectin (FC)

End point title	Change from Baseline in Fecal Calprotectin (FC)

End point description:

Change from baseline in FC were reported. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (that is, first 48 weeks of the study). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. Here, 'N' (Number analysed) included subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	189		
Units: Micrograms per gram (mcg/g)				
arithmetic mean (standard deviation)				
Change at Week 16	-988.8 (± 3243.61)	-728.2 (± 2238.60)		
Change at Week 48	-1191.6 (± 3441.64)	-744.4 (± 2589.30)		
Change at Endpoint (LOCF)	-1191.6 (± 3441.64)	-744.4 (± 2589.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Inflammatory Bowel Disease Questionnaire (IBDQ) Response

End point title	Percentage of Subjects with Inflammatory Bowel Disease Questionnaire (IBDQ) Response

End point description:

The IBDQ is 32-item questionnaire for subjects with Inflammatory Bowel Disease (IBD) used to evaluate disease-specific health-related quality of life. IBDQ consists of 32 items, each item score ranged from 1 (worst possible response) to 7 (best possible response). The 32 items were grouped into 4 domains: bowel function, emotional status, systemic symptoms and social function. The 4 domains were scored as follows: 10 to 70 (bowel symptoms); 5 to 35 (systemic symptoms); 12 to 84 (emotional function); and 5 to 35 (social function). For each domain, higher score indicated better quality of life. Total score is sum of each item score and ranges from 32 to 224. Higher score means better quality of life. FRAS was used. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (that is, first 48 weeks).

End point type	Secondary

End point timeframe:

Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16	71.7 (65.2 to 77.6)	75.1 (68.9 to 80.7)		
Week 48	58.4 (51.6 to 65.0)	67.0 (60.3 to 73.1)		

Endpoint (LOCF)	77.2 (71.0 to 82.6)	77.8 (71.8 to 83.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Work Productivity and Activity Impairment (WPAI) Scores for Each Domain

End point title	Percentage of Subjects With Work Productivity and Activity Impairment (WPAI) Scores for Each Domain

End point description:

The WPAI questionnaire is a well-validated instrument of 6-item questionnaire with a 7-day recall period. The WPAI questionnaire produces 4 types of scores: absenteeism (work time missed), presenteesism (impairment at work/reduced on-the-job effectiveness), work productivity loss (overall work impairment/absenteeism plus presenteeism), and activity impairment. Each score ranges from 0 to 100. The WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, worse outcomes. FRAS was used. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint defined as last available postbaseline result within main analysis period (i.e, first 48 weeks). Here 'N' (Number analysed) refers subjects evaluable for this endpoint and 'n' (number analysed) refers to subjects analysed for specified categories. Subjects with missing data were analysed as no improvement.

End point type	Secondary

End point timeframe:

Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	215		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 16: Absenteeism (n=86,96)	34.9 (24.9 to 45.9)	39.6 (29.7 to 50.1)		
Week 48: Absenteeism (n=60,77)	35.0 (23.1 to 48.4)	36.4 (25.7 to 48.1)		
Endpoint: Absenteeism (n=83,91)	34.9 (24.8 to 46.2)	36.3 (26.4 to 47.0)		
Week 16: Presenteeism (n=105,104)	70.5 (60.8 to 79.0)	76.9 (67.6 to 84.6)		
Week 48: Presenteeism (n=78,92)	73.1 (61.8 to 82.5)	72.8 (62.6 to 81.6)		
Endpoint: Presenteeism (n=102,106)	69.6 (59.7 to 78.3)	69.8 (60.1 to 78.3)		
Week 16: Work Productivity Loss (n=77,82)	71.4 (60.0 to 81.2)	70.7 (59.6 to 80.3)		
Week 48: Work Productivity Loss (n=56,68)	75.0 (61.6 to 85.6)	72.1 (59.9 to 82.3)		
Endpoint: Work Productivity Loss (n=76,79)	72.4 (60.9 to 82.0)	69.6 (58.2 to 79.5)		

Week 16: Activity Impairment (n=204,207)	72.1 (65.4 to 78.1)	78.3 (72.0 to 83.7)		
Week 48: Activity Impairment (n=156,178)	74.4 (66.8 to 81.0)	71.9 (64.7 to 78.4)		
Endpoint: Activity Impairment (n=212,215)	67.9 (61.2 to 74.2)	70.7 (64.1 to 76.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in IBDQ Score

End point title	Change From Baseline in IBDQ Score

End point description:

The IBDQ is 32-item questionnaire used to evaluate disease-specific health-related quality of life. Each item score ranged from 1 (worst possible response) to 7 (best possible response). Items were grouped into 4 domains: bowel function, emotional status, systemic symptoms and social function with scored as follows: 10 to 70 (bowel symptoms); 5 to 35 (systemic symptoms); 12 to 84 (emotional function); and 5 to 35 (social function). Higher score, better quality of life. Total score is sum of each item score and ranges from 32 to 224. FRAS was used. LOCF:subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint defined as last available postbaseline result within main analysis period (i.e first 48 weeks). Here, N (Number analysed) refers subjects evaluable for this endpoint. Only subjects with non-missing baseline value and at least one non-missing post-baseline value during main treatment period were included in analysis.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	217		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 16	41.3 (± 34.24)	44.7 (± 33.20)		
Change at Week 48	43.7 (± 35.16)	44.3 (± 36.94)		
Change at Endpoint (LOCF)	43.7 (± 35.16)	44.3 (± 36.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality Of Life 5 Dimensions 5 Level (EQ-5D-5L) Score

End point title	Change From Baseline in European Quality Of Life 5 Dimensions 5 Level (EQ-5D-5L) Score

End point description:

The EQ-5D-5L is a validated quality-of-life instrument which consists of the EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). A descriptive system comprises 5 dimensions of health

(mobility, self -care, usual activities, pain/discomfort, and anxiety/depression) to describe the subject current health state. Each dimension comprises 5 levels with corresponding numeric scores, where 1 indicates no problems, and 5 indicates extreme problems. Higher scores representing a better health state. EQ-VAS self-rating records respondent's own assessment of his/her overall health status at time of completion, on scale of 0 (worst health) to 100 (best health). FRAS was used. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks). Here, N (Number analysed) refers subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	218	218		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 16	16.7 (± 20.19)	18.7 (± 20.16)		
Change at Week 48	16.5 (± 22.77)	16.1 (± 21.71)		
Change at Endpoint (LOCF)	16.5 (± 22.77)	16.1 (± 21.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes From Baseline in Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-F) Scale Score

End point title	Changes From Baseline in Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-F) Scale Score

End point description:

The FACIT-F scale is a 13-item fatigue scale with a 7-day recall period. It measures the level of fatigue during the usual daily activities. The level of fatigue is measured on a 4-point Likert scale (0=very much fatigued to 4=not at all fatigued). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worst score) to 52 (best score). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks of the study). Here, 'N' (Number analysed) included subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	220		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 16	9.1 (± 10.57)	11.6 (± 10.12)		
Change at Week 48	9.9 (± 11.35)	10.0 (± 11.11)		
Change at Endpoint (LOCF)	9.9 (± 11.35)	10.0 (± 11.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hospital Anxiety and Depression Scale (HADS)

End point title	Change From Baseline in Hospital Anxiety and Depression Scale (HADS)

End point description:

The HADS is a validated 14-item scale with 7 of the items relating to anxiety and 7 relating to depression. Each item is scored from 0 to 3, with higher scores indicating greater likelihood of depression or anxiety. Cases of anxiety or depression are each defined by subscale scores of 8 or greater and categorized as normal (score of 0 to 7), mild (score of 8 to 10), moderate (score of 11 to 14), and severe (score of 15 to 21). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks of the study). Here, 'N' (Number analysed) included subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	217		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Anxiety: Change at Week 16	-2.5 (± 3.43)	-2.5 (± 3.88)		
Depression: Change at Week 16	-2.5 (± 3.59)	-2.4 (± 3.41)		
Anxiety: Change at Week 48	-2.5 (± 3.64)	-2.7 (± 4.05)		
Depression: Change at Week 48	-2.4 (± 4.00)	-2.2 (± 3.97)		
Anxiety: Change at Endpoint (LOCF)	-2.5 (± 3.64)	-2.7 (± 4.05)		
Depression: Change at Endpoint (LOCF)	-2.4 (± 4.00)	-2.2 (± 3.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WPAI Score

End point title	Change From Baseline in WPAI Score

End point description:

The WPAI questionnaire is a well-validated instrument with 6-item questionnaire with a 7-day recall period. The WPAI questionnaire produces 4 types of scores: absenteeism (work time missed), presenteesism (impairment at work/reduced on-the-job effectiveness), work productivity loss (overall work impairment/absenteeism plus presenteeism), and activity impairment. Each score ranges from 0 to 100 with higher scores indicating greater impairment and less productivity. FRAS population was used. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks). Here, 'N' (Number analysed) refers subjects evaluable for this endpoint and 'n' (number analysed) refers subjects analysed for specified categories.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	215		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Absenteeism: Change at Week 16 (n=86,96)	-12.9 (± 31.39)	-12.5 (± 30.86)		
Absenteeism: Change at Week 48 (n=60,77)	-13.9 (± 34.13)	-14.8 (± 30.22)		
Absenteeism: Change at Endpoint (n=83, 91)	-13.0 (± 34.87)	-12.1 (± 31.92)		
Presenteeism: Change at Week 16: (n=105,104)	-23.3 (± 27.76)	-26.2 (± 30.09)		
Presenteeism: Change at Week 48: (n=78,92)	-30.0 (± 31.83)	-26.0 (± 28.90)		
Presenteeism: Change at Endpoint: (n=102,106)	-26.5 (± 30.50)	-22.5 (± 30.99)		
Work Productivity Loss: Change at Week 16(n=77,82)	-25.2 (± 27.71)	-27.2 (± 31.79)		
Work Productivity Loss: Change at Week 48(n=56,68)	-33.0 (± 33.98)	-28.0 (± 31.66)		
Work Productivity Loss:Change at Endpoint(n=76,79)	-29.1 (± 32.91)	-24.1 (± 33.97)		
Activity Impairment: Change at Week 16(n=204,207)	-24.1 (± 27.23)	-27.3 (± 26.77)		
Activity Impairment: Change at Week 48(n=156,178)	-29.2 (± 29.65)	-24.8 (± 28.96)		
Activity Impairment:Change at Endpoint(n=212, 215)	-25.5 (± 29.13)	-23.6 (± 29.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time Lost From Work

End point title	Change From Baseline in Time Lost From Work

End point description:

Time lost from work was collected by asking the subjects a single question, "How many days did you miss from work due to your Crohn's disease in the last 4 weeks?" FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks of the study). Here, 'N' (Number analysed) included subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	139		
Units: Days				
arithmetic mean (standard deviation)				
Change at Week 16	-1.7 (± 4.32)	-1.8 (± 6.03)		
Change at Week 48	-1.8 (± 4.58)	-2.2 (± 5.99)		
Change at Endpoint (LOCF)	-1.8 (± 4.58)	-2.2 (± 5.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs) That Occurred in Subjects Administered with Ustekinumab up to Week 48

End point title	Number of Subjects With Adverse Events (AEs) That Occurred in Subjects Administered with Ustekinumab up to Week 48

End point description:

An adverse event is any untoward medical event that occurs in subjects administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Subjects	188	179		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Weight

End point title	Change from Baseline in Body Weight

End point description:

Change from baseline in body weight were reported. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Kilograms (Kg)				
arithmetic mean (standard deviation)				
Change at Week 16	1.56 (± 2.996)	1.16 (± 3.586)		
Change at Week 48	2.38 (± 4.682)	1.39 (± 4.877)		
Change at Endpoint (LOCF)	2.38 (± 4.682)	1.39 (± 4.877)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Mass index (BMI)

End point title	Change from Baseline in Body Mass index (BMI)

End point description:

Change from baseline in BMI were reported. BMI is a person’s weight (in kilograms) divided by the square of height (in meters). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks).

End point type	Secondary

End point timeframe:

Baseline, Weeks 16 and 48, Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Kilogram per meter square (Kg/m^2)				
arithmetic mean (standard deviation)				
Change at Week 16	0.54 (± 1.052)	0.37 (± 1.236)		
Change at Week 48	0.82 (± 1.622)	0.46 (± 1.665)		
Change at Endpoint (LOCF)	0.82 (± 1.622)	0.46 (± 1.665)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Blood Pressure

End point title	Change from Baseline in Blood Pressure

End point description:

Change from baseline in Blood Pressure (Systolic Blood Pressure [SPB] and Diastolic Blood Pressure [DBP]) were reported. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks). FRAS included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP: Change at Week 16	2.3 (± 13.16)	0.3 (± 12.59)		
SBP: Change at Week 48	1.9 (± 13.21)	0.5 (± 12.47)		
SBP: Change at Endpoint (LOCF)	1.9 (± 13.21)	0.5 (± 12.47)		
DBP: Change at Week 16	1.1 (± 9.46)	0.8 (± 9.81)		
DBP: Change at Week 48	1.2 (± 10.02)	0.6 (± 9.85)		
DBP: Change at Endpoint (LOCF)	1.2 (± 10.02)	0.6 (± 9.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate

End point title	Change from Baseline in Pulse Rate

End point description:

Change from baseline in pulse rate were reported. LOCF: subjects who had missing SES-CD score or stopped treatment before Week 48 had last SES-CD score carried forward. Endpoint is defined as the last available postbaseline result within the main analysis period (i.e. first 48 weeks). FRAS set included all subjects who received at least 1 dose of study agent and were randomized at Week 16, regardless of study treatment being administered once randomised.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, and Endpoint (LOCF)

End point values	Treat to Target	Routine Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	221		
Units: Beats/minutes				
arithmetic mean (standard deviation)				
Change at Week 16	-1.5 (± 11.98)	-2.0 (± 11.51)		
Change at Week 48	-0.2 (± 13.39)	-1.7 (± 12.16)		
Change at Endpoint (LOCF)	-0.2 (± 13.39)	-1.7 (± 12.16)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Induction Period= Baseline up to Week 16; Maintenance Period= Baseline up to Week 48; Extension Period/End of Study= Baseline up to Week 104

Adverse event reporting additional description:

Induction period: Safety analysis set included subjects from FAS. Maintenance period: FRAS included subjects who got at least 1 dose of drug and randomised at Week 16, regardless of study treatment received once randomized. Extension period: Modified FAS included subjects randomised at Week 16 that completed Week 48 and entered extension period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Maintenance Period: Treat to Target

Reporting group description:

Subjects with less than (<) 25 percent (%) improvement in simple endoscopic score for Crohn's disease (SES-CD) at Week 16 versus baseline received ustekinumab 90 mg SC dose 8-weekly maintenance treatment while subjects with >= 25% improvement in SES-CD score at Week 16 versus baseline received ustekinumab 90 mg SC dose 12-weekly treatment based on centrally-read ileocolonoscopy findings. From Week 24 for subjects assigned to the 8-weekly regimen or from Week 20 for the 12-weekly regimen group ustekinumab 90 mg SC maintenance treatment was directed by treat to target assessments based on C-reactive protein (CRP) and CDAI assessments. Subjects previously on 12-weekly regimens were adjusted to 8-weekly dosing; those previously on 8-weekly regimens were adjusted to 4-weekly dosing. Subjects subsequently failing to meet treatment targets at the next assessment visit 4 weeks after dosing were not able to optimize dosing further and left the study.

Reporting group title	Induction Period

Reporting group description:

Subjects were administered with approximately 6 mg/kg intravenous (IV) injection of ustekinumab at Week 0 and 90 mg subcutaneous (SC) injection of ustekinumab at Week 8. At Week 16, subjects who did not achieve a Crohn's Disease Activity Index (CDAI) improvement (non-responders) of greater than or equal to (>=) 70 points versus Week 0 (CDAI-70), left the study. Subjects who achieved CDAI improvement (responders) of at least 70 points versus Week 0 were randomised in open-label maintenance period either with treat to target arm or routine care arm.

Reporting group title	Extension Period: Treat to Target

Reporting group description:

From Week 48, subjects continued to received SC ustekinumab 90 mg in the long-term extension (LTE) period up to Week 104. The frequency of ustekinumab dosing with escalation/de-escalation between once in 12 weeks (q12w)/q8w/q4w was based on the following targets: endoscopic remission (CD [SES-CD] score less than or equal to [<=] 2) and corticosteroid (CS)-free clinical remission (CDAI score of <150 points of >=16 weeks duration) at Week 48; and later, on CS-free clinical remission and biomarker remission (C-reactive protein <=10 miligrams per liter [mg/L] and fecal calprotectin <=250 micrograms per gram [mcg/g]) at 2 consecutive visits 8 weeks apart. Subjects on q4w dosing failing to reach targets were discontinued.

Reporting group title	Extension Period: Routine Care

Reporting group description:

From Week 48, subjects continued to received SC ustekinumab 90 mg in the long-term extension (LTE) period up to Week 104. The frequency of ustekinumab dosing with escalation/de-escalation between once in 12 weeks (q12w)/q8w/q4w was based on the following targets: endoscopic remission (CD [SES-CD] score <=2) and corticosteroid (CS)-free clinical remission (CDAI score of <150 points of >=16 weeks duration) at Week 48; and later, on CS-free clinical remission and biomarker remission (C-reactive protein <=10 mg/L and fecal calprotectin <=250 mcg/g) at 2 consecutive visits 8 weeks apart. Subjects on q4w dosing failing to reach targets were discontinued.

Reporting group title	Maintenance Period: Routine Care

Reporting group description:

Subjects received ustekinumab 90 mg SC dose every 8-weeks or every 12-weeks according to clinical judgment. At Week 16, (that is, 8 weeks after the first SC dose), subjects who did not show adequate

response based on the investigator's judgment received a second ustekinumab 90 mg SC dose at that time. Clinical assessments in case of disease flare were performed at investigator's discretion. Subjects who lost response during 12-weekly could adjust the dosing to 8-weekly maintenance treatment. Subjects previously received 8-weekly ustekinumab treatment were unable to adjust the dose following disease flare and left the study as per investigator's judgment.

Serious adverse events	Maintenance Period: Treat to Target	Induction Period	Extension Period: Treat to Target
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 219 (11.87%)	28 / 498 (5.62%)	21 / 147 (14.29%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix Neoplasm			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive Ductal Breast Carcinoma			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Adenocarcinoma			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant Melanoma			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine Carcinoma Metastatic			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma Cell Myeloma			

subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial Spreading Melanoma Stage Unspecified			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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 Death			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Female Genital Tract Fistula			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal Pain			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Psychiatric disorders			
Major Depression			

subjects affected / exposed	1 / 219 (0.46%)	2 / 498 (0.40%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Body Temperature Increased			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Head Injury			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint Dislocation			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Acute			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Dizziness Exertional			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Temporal Lobe Epilepsy			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Eye disorders			
Cataract			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal Fistula			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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	4 / 219 (1.83%)	6 / 498 (1.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of Small Intestine			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Ileus			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Intestinal Obstruction			

subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Intestinal Perforation			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Intestinal Stenosis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-Abdominal Fluid Collection			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Large Intestine Perforation			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Large Intestine Polyp			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Pancreatitis Acute			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Vomiting			

subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back Pain			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	0 / 147 (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
Osteitis			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal Wall Abscess			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess Intestinal			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (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
Anal Abscess			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholinitis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter Infection			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 Pneumonia			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis Infectious			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			

subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Gastroenteritis			
subjects affected / exposed	1 / 219 (0.46%)	2 / 498 (0.40%)	0 / 147 (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
Infectious Colitis			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Large Intestine Infection			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal Abscess			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (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
Pharyngitis			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	1 / 147 (0.68%)
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	Extension Period: Routine Care	Maintenance Period: Routine Care	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 176 (13.07%)	29 / 221 (13.12%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix Neoplasm			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Invasive Ductal Breast Carcinoma			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Adenocarcinoma			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine Carcinoma Metastatic			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma Cell Myeloma			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial Spreading Melanoma Stage Unspecified			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Death			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Female Genital Tract Fistula			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metrorrhagia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal Pain			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major Depression			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide Attempt			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Body Temperature Increased			

subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head Injury			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Dislocation			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure Acute			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness Exertional			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Temporal Lobe Epilepsy			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	2 / 176 (1.14%)	2 / 221 (0.90%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Fistula			
subjects affected / exposed	1 / 176 (0.57%)	2 / 221 (0.90%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
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	4 / 176 (2.27%)	8 / 221 (3.62%)	
occurrences causally related to treatment / all	1 / 4	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula of Small Intestine			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Perforation			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Stenosis			

subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-Abdominal Fluid Collection			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Polyp			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	2 / 176 (1.14%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			

subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Wall Abscess			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Intestinal			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anal Abscess			
subjects affected / exposed	1 / 176 (0.57%)	3 / 221 (1.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholinitis			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter Infection			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19 Pneumonia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis Infectious			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious Colitis			

subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Infection			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal Abscess			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Maintenance Period: Treat to Target	Induction Period	Extension Period: Treat to Target
Total subjects affected by non-serious adverse events			
subjects affected / exposed	158 / 219 (72.15%)	238 / 498 (47.79%)	125 / 147 (85.03%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 219 (0.46%)	3 / 498 (0.60%)	2 / 147 (1.36%)
occurrences (all)	1	3	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 219 (3.65%)	10 / 498 (2.01%)	10 / 147 (6.80%)
occurrences (all)	8	10	12
Fatigue			

subjects affected / exposed	2 / 219 (0.91%)	3 / 498 (0.60%)	1 / 147 (0.68%)
occurrences (all)	2	3	1
Influenza Like Illness			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	4 / 147 (2.72%)
occurrences (all)	1	1	7
Pyrexia			
subjects affected / exposed	25 / 219 (11.42%)	25 / 498 (5.02%)	15 / 147 (10.20%)
occurrences (all)	37	33	25
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 219 (1.37%)	4 / 498 (0.80%)	3 / 147 (2.04%)
occurrences (all)	3	4	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 219 (3.65%)	6 / 498 (1.20%)	6 / 147 (4.08%)
occurrences (all)	9	6	8
Oropharyngeal Pain			
subjects affected / exposed	5 / 219 (2.28%)	2 / 498 (0.40%)	8 / 147 (5.44%)
occurrences (all)	8	2	11
Productive Cough			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences (all)	1	1	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 219 (1.83%)	2 / 498 (0.40%)	2 / 147 (1.36%)
occurrences (all)	4	2	2
Depression			
subjects affected / exposed	0 / 219 (0.00%)	3 / 498 (0.60%)	1 / 147 (0.68%)
occurrences (all)	0	3	1
Insomnia			
subjects affected / exposed	4 / 219 (1.83%)	1 / 498 (0.20%)	4 / 147 (2.72%)
occurrences (all)	4	1	6
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences (all)	0	0	0

C-Reactive Protein Increased			
subjects affected / exposed	4 / 219 (1.83%)	6 / 498 (1.20%)	3 / 147 (2.04%)
occurrences (all)	4	6	3
Serum Ferritin Decreased			
subjects affected / exposed	2 / 219 (0.91%)	0 / 498 (0.00%)	5 / 147 (3.40%)
occurrences (all)	2	0	6
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 219 (0.91%)	2 / 498 (0.40%)	3 / 147 (2.04%)
occurrences (all)	2	2	3
Ligament Sprain			
subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	2 / 147 (1.36%)
occurrences (all)	1	1	2
Procedural Pain			
subjects affected / exposed	2 / 219 (0.91%)	0 / 498 (0.00%)	3 / 147 (2.04%)
occurrences (all)	2	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 219 (10.96%)	36 / 498 (7.23%)	20 / 147 (13.61%)
occurrences (all)	42	47	62
Migraine			
subjects affected / exposed	0 / 219 (0.00%)	3 / 498 (0.60%)	0 / 147 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 219 (3.65%)	14 / 498 (2.81%)	8 / 147 (5.44%)
occurrences (all)	10	14	10
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 219 (1.37%)	3 / 498 (0.60%)	3 / 147 (2.04%)
occurrences (all)	3	3	3
Eye disorders			
Cataract			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	3 / 147 (2.04%)
occurrences (all)	1	0	3
Dry Eye			

subjects affected / exposed	1 / 219 (0.46%)	2 / 498 (0.40%)	1 / 147 (0.68%)
occurrences (all)	1	2	1
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	3 / 219 (1.37%)	5 / 498 (1.00%)	3 / 147 (2.04%)
occurrences (all)	4	5	5
Abdominal Pain			
subjects affected / exposed	23 / 219 (10.50%)	18 / 498 (3.61%)	23 / 147 (15.65%)
occurrences (all)	31	26	36
Abdominal Pain Upper			
subjects affected / exposed	7 / 219 (3.20%)	6 / 498 (1.20%)	7 / 147 (4.76%)
occurrences (all)	7	7	8
Anal Fissure			
subjects affected / exposed	1 / 219 (0.46%)	3 / 498 (0.60%)	1 / 147 (0.68%)
occurrences (all)	1	3	1
Anal Fistula			
subjects affected / exposed	2 / 219 (0.91%)	2 / 498 (0.40%)	3 / 147 (2.04%)
occurrences (all)	2	2	4
Constipation			
subjects affected / exposed	4 / 219 (1.83%)	7 / 498 (1.41%)	4 / 147 (2.72%)
occurrences (all)	5	8	5
Crohn's Disease			
subjects affected / exposed	16 / 219 (7.31%)	9 / 498 (1.81%)	18 / 147 (12.24%)
occurrences (all)	17	10	19
Diarrhoea			
subjects affected / exposed	11 / 219 (5.02%)	9 / 498 (1.81%)	17 / 147 (11.56%)
occurrences (all)	13	10	21
Dyspepsia			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	1 / 147 (0.68%)
occurrences (all)	1	0	1
Flatulence			
subjects affected / exposed	4 / 219 (1.83%)	0 / 498 (0.00%)	4 / 147 (2.72%)
occurrences (all)	5	0	6
Frequent Bowel Movements			
subjects affected / exposed	2 / 219 (0.91%)	3 / 498 (0.60%)	1 / 147 (0.68%)
occurrences (all)	2	3	1

Gastrooesophageal Reflux Disease			
subjects affected / exposed	4 / 219 (1.83%)	2 / 498 (0.40%)	3 / 147 (2.04%)
occurrences (all)	4	2	3
Haematochezia			
subjects affected / exposed	2 / 219 (0.91%)	0 / 498 (0.00%)	2 / 147 (1.36%)
occurrences (all)	2	0	3
Haemorrhoids			
subjects affected / exposed	2 / 219 (0.91%)	1 / 498 (0.20%)	1 / 147 (0.68%)
occurrences (all)	2	1	1
Nausea			
subjects affected / exposed	12 / 219 (5.48%)	12 / 498 (2.41%)	11 / 147 (7.48%)
occurrences (all)	18	16	13
Toothache			
subjects affected / exposed	5 / 219 (2.28%)	3 / 498 (0.60%)	6 / 147 (4.08%)
occurrences (all)	6	3	7
Vomiting			
subjects affected / exposed	9 / 219 (4.11%)	7 / 498 (1.41%)	5 / 147 (3.40%)
occurrences (all)	10	10	6
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 219 (2.28%)	6 / 498 (1.20%)	4 / 147 (2.72%)
occurrences (all)	5	6	4
Eczema			
subjects affected / exposed	4 / 219 (1.83%)	3 / 498 (0.60%)	4 / 147 (2.72%)
occurrences (all)	4	3	5
Erythema			
subjects affected / exposed	4 / 219 (1.83%)	4 / 498 (0.80%)	4 / 147 (2.72%)
occurrences (all)	4	5	6
Pruritus			
subjects affected / exposed	4 / 219 (1.83%)	4 / 498 (0.80%)	5 / 147 (3.40%)
occurrences (all)	4	4	5
Rash			
subjects affected / exposed	5 / 219 (2.28%)	3 / 498 (0.60%)	9 / 147 (6.12%)
occurrences (all)	6	3	10
Skin Lesion			

subjects affected / exposed	1 / 219 (0.46%)	1 / 498 (0.20%)	3 / 147 (2.04%)
occurrences (all)	1	1	3
Renal and urinary disorders			
Renal Colic			
subjects affected / exposed	2 / 219 (0.91%)	0 / 498 (0.00%)	3 / 147 (2.04%)
occurrences (all)	2	0	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 219 (10.96%)	29 / 498 (5.82%)	24 / 147 (16.33%)
occurrences (all)	30	31	29
Arthritis			
subjects affected / exposed	4 / 219 (1.83%)	2 / 498 (0.40%)	3 / 147 (2.04%)
occurrences (all)	4	2	3
Back Pain			
subjects affected / exposed	7 / 219 (3.20%)	11 / 498 (2.21%)	15 / 147 (10.20%)
occurrences (all)	8	11	17
Myalgia			
subjects affected / exposed	5 / 219 (2.28%)	6 / 498 (1.20%)	6 / 147 (4.08%)
occurrences (all)	7	7	8
Neck Pain			
subjects affected / exposed	1 / 219 (0.46%)	3 / 498 (0.60%)	2 / 147 (1.36%)
occurrences (all)	1	3	2
Pain in Extremity			
subjects affected / exposed	2 / 219 (0.91%)	1 / 498 (0.20%)	3 / 147 (2.04%)
occurrences (all)	2	1	3
Infections and infestations			
Anal Abscess			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	0 / 147 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	4 / 219 (1.83%)	5 / 498 (1.00%)	4 / 147 (2.72%)
occurrences (all)	7	5	7
Gastroenteritis			
subjects affected / exposed	7 / 219 (3.20%)	5 / 498 (1.00%)	12 / 147 (8.16%)
occurrences (all)	7	5	12
Covid-19			

subjects affected / exposed	0 / 219 (0.00%)	0 / 498 (0.00%)	5 / 147 (3.40%)
occurrences (all)	0	0	5
Gastroenteritis Viral			
subjects affected / exposed	4 / 219 (1.83%)	1 / 498 (0.20%)	3 / 147 (2.04%)
occurrences (all)	4	1	3
Gastrointestinal Infection			
subjects affected / exposed	1 / 219 (0.46%)	0 / 498 (0.00%)	3 / 147 (2.04%)
occurrences (all)	1	0	3
Influenza			
subjects affected / exposed	12 / 219 (5.48%)	13 / 498 (2.61%)	14 / 147 (9.52%)
occurrences (all)	13	13	15
Nasopharyngitis			
subjects affected / exposed	29 / 219 (13.24%)	44 / 498 (8.84%)	23 / 147 (15.65%)
occurrences (all)	48	48	46
Oral Herpes			
subjects affected / exposed	5 / 219 (2.28%)	6 / 498 (1.20%)	4 / 147 (2.72%)
occurrences (all)	5	6	6
Pharyngitis			
subjects affected / exposed	9 / 219 (4.11%)	3 / 498 (0.60%)	7 / 147 (4.76%)
occurrences (all)	11	3	9
Sinusitis			
subjects affected / exposed	3 / 219 (1.37%)	5 / 498 (1.00%)	1 / 147 (0.68%)
occurrences (all)	4	5	1
Rhinitis			
subjects affected / exposed	3 / 219 (1.37%)	2 / 498 (0.40%)	1 / 147 (0.68%)
occurrences (all)	3	2	1
Tonsillitis			
subjects affected / exposed	3 / 219 (1.37%)	2 / 498 (0.40%)	5 / 147 (3.40%)
occurrences (all)	3	2	7
Tooth Abscess			
subjects affected / exposed	3 / 219 (1.37%)	1 / 498 (0.20%)	6 / 147 (4.08%)
occurrences (all)	4	1	7
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 219 (1.83%)	6 / 498 (1.20%)	4 / 147 (2.72%)
occurrences (all)	6	7	6
Urinary Tract Infection			

subjects affected / exposed	3 / 219 (1.37%)	5 / 498 (1.00%)	5 / 147 (3.40%)
occurrences (all)	3	5	5
Vaginal Infection			
subjects affected / exposed	2 / 219 (0.91%)	0 / 498 (0.00%)	3 / 147 (2.04%)
occurrences (all)	2	0	3
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	4 / 219 (1.83%)	4 / 498 (0.80%)	2 / 147 (1.36%)
occurrences (all)	4	4	2
Folate Deficiency			
subjects affected / exposed	2 / 219 (0.91%)	1 / 498 (0.20%)	4 / 147 (2.72%)
occurrences (all)	2	1	4
Hypokalaemia			
subjects affected / exposed	0 / 219 (0.00%)	1 / 498 (0.20%)	0 / 147 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	3 / 219 (1.37%)	2 / 498 (0.40%)	3 / 147 (2.04%)
occurrences (all)	3	2	4
Iron Deficiency			
subjects affected / exposed	3 / 219 (1.37%)	2 / 498 (0.40%)	3 / 147 (2.04%)
occurrences (all)	3	2	3
Vitamin B12 Deficiency			
subjects affected / exposed	3 / 219 (1.37%)	1 / 498 (0.20%)	6 / 147 (4.08%)
occurrences (all)	3	1	6
Vitamin D Deficiency			
subjects affected / exposed	3 / 219 (1.37%)	2 / 498 (0.40%)	6 / 147 (4.08%)
occurrences (all)	5	2	9

Non-serious adverse events	Extension Period: Routine Care	Maintenance Period: Routine Care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	135 / 176 (76.70%)	150 / 221 (67.87%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 176 (2.84%)	4 / 221 (1.81%)	
occurrences (all)	5	4	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	8 / 176 (4.55%)	6 / 221 (2.71%)	
occurrences (all)	8	6	
Fatigue			
subjects affected / exposed	5 / 176 (2.84%)	7 / 221 (3.17%)	
occurrences (all)	6	8	
Influenza Like Illness			
subjects affected / exposed	2 / 176 (1.14%)	0 / 221 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	26 / 176 (14.77%)	19 / 221 (8.60%)	
occurrences (all)	35	21	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 176 (0.57%)	2 / 221 (0.90%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 176 (6.82%)	7 / 221 (3.17%)	
occurrences (all)	15	8	
Oropharyngeal Pain			
subjects affected / exposed	9 / 176 (5.11%)	5 / 221 (2.26%)	
occurrences (all)	9	5	
Productive Cough			
subjects affected / exposed	4 / 176 (2.27%)	1 / 221 (0.45%)	
occurrences (all)	4	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	6 / 176 (3.41%)	3 / 221 (1.36%)	
occurrences (all)	6	3	
Depression			
subjects affected / exposed	4 / 176 (2.27%)	5 / 221 (2.26%)	
occurrences (all)	4	5	
Insomnia			
subjects affected / exposed	5 / 176 (2.84%)	3 / 221 (1.36%)	
occurrences (all)	5	3	

Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	4 / 176 (2.27%)	3 / 221 (1.36%)	
occurrences (all)	4	3	
C-Reactive Protein Increased			
subjects affected / exposed	1 / 176 (0.57%)	2 / 221 (0.90%)	
occurrences (all)	2	2	
Serum Ferritin Decreased			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 176 (1.14%)	2 / 221 (0.90%)	
occurrences (all)	2	2	
Ligament Sprain			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Procedural Pain			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 176 (15.91%)	21 / 221 (9.50%)	
occurrences (all)	92	51	
Migraine			
subjects affected / exposed	6 / 176 (3.41%)	2 / 221 (0.90%)	
occurrences (all)	6	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 176 (4.55%)	11 / 221 (4.98%)	
occurrences (all)	10	13	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 176 (0.00%)	2 / 221 (0.90%)	
occurrences (all)	0	2	
Eye disorders			

Cataract			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences (all)	0	1	
Dry Eye			
subjects affected / exposed	4 / 176 (2.27%)	3 / 221 (1.36%)	
occurrences (all)	5	3	
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	6 / 176 (3.41%)	6 / 221 (2.71%)	
occurrences (all)	8	7	
Abdominal Pain			
subjects affected / exposed	22 / 176 (12.50%)	17 / 221 (7.69%)	
occurrences (all)	34	22	
Abdominal Pain Upper			
subjects affected / exposed	4 / 176 (2.27%)	4 / 221 (1.81%)	
occurrences (all)	8	6	
Anal Fissure			
subjects affected / exposed	4 / 176 (2.27%)	6 / 221 (2.71%)	
occurrences (all)	5	6	
Anal Fistula			
subjects affected / exposed	3 / 176 (1.70%)	4 / 221 (1.81%)	
occurrences (all)	4	5	
Constipation			
subjects affected / exposed	6 / 176 (3.41%)	6 / 221 (2.71%)	
occurrences (all)	7	7	
Crohn's Disease			
subjects affected / exposed	20 / 176 (11.36%)	21 / 221 (9.50%)	
occurrences (all)	22	24	
Diarrhoea			
subjects affected / exposed	17 / 176 (9.66%)	13 / 221 (5.88%)	
occurrences (all)	24	15	
Dyspepsia			
subjects affected / exposed	5 / 176 (2.84%)	3 / 221 (1.36%)	
occurrences (all)	9	7	
Flatulence			

subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Frequent Bowel Movements			
subjects affected / exposed	5 / 176 (2.84%)	3 / 221 (1.36%)	
occurrences (all)	5	3	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Haematochezia			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Haemorrhoids			
subjects affected / exposed	6 / 176 (3.41%)	3 / 221 (1.36%)	
occurrences (all)	8	3	
Nausea			
subjects affected / exposed	16 / 176 (9.09%)	12 / 221 (5.43%)	
occurrences (all)	21	15	
Toothache			
subjects affected / exposed	4 / 176 (2.27%)	4 / 221 (1.81%)	
occurrences (all)	4	5	
Vomiting			
subjects affected / exposed	11 / 176 (6.25%)	9 / 221 (4.07%)	
occurrences (all)	12	12	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 176 (2.27%)	4 / 221 (1.81%)	
occurrences (all)	4	4	
Eczema			
subjects affected / exposed	2 / 176 (1.14%)	1 / 221 (0.45%)	
occurrences (all)	2	1	
Erythema			
subjects affected / exposed	4 / 176 (2.27%)	3 / 221 (1.36%)	
occurrences (all)	5	4	
Pruritus			
subjects affected / exposed	2 / 176 (1.14%)	2 / 221 (0.90%)	
occurrences (all)	3	3	

Rash			
subjects affected / exposed	7 / 176 (3.98%)	7 / 221 (3.17%)	
occurrences (all)	9	8	
Skin Lesion			
subjects affected / exposed	0 / 176 (0.00%)	1 / 221 (0.45%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal Colic			
subjects affected / exposed	1 / 176 (0.57%)	2 / 221 (0.90%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 176 (14.77%)	19 / 221 (8.60%)	
occurrences (all)	35	22	
Arthritis			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences (all)	1	0	
Back Pain			
subjects affected / exposed	18 / 176 (10.23%)	12 / 221 (5.43%)	
occurrences (all)	25	12	
Myalgia			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	5	2	
Neck Pain			
subjects affected / exposed	7 / 176 (3.98%)	4 / 221 (1.81%)	
occurrences (all)	13	4	
Pain in Extremity			
subjects affected / exposed	1 / 176 (0.57%)	0 / 221 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Anal Abscess			
subjects affected / exposed	5 / 176 (2.84%)	3 / 221 (1.36%)	
occurrences (all)	5	3	
Bronchitis			
subjects affected / exposed	11 / 176 (6.25%)	8 / 221 (3.62%)	
occurrences (all)	15	10	

Gastroenteritis			
subjects affected / exposed	9 / 176 (5.11%)	5 / 221 (2.26%)	
occurrences (all)	9	5	
Covid-19			
subjects affected / exposed	3 / 176 (1.70%)	0 / 221 (0.00%)	
occurrences (all)	3	0	
Gastroenteritis Viral			
subjects affected / exposed	5 / 176 (2.84%)	3 / 221 (1.36%)	
occurrences (all)	5	3	
Gastrointestinal Infection			
subjects affected / exposed	2 / 176 (1.14%)	0 / 221 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	14 / 176 (7.95%)	11 / 221 (4.98%)	
occurrences (all)	16	12	
Nasopharyngitis			
subjects affected / exposed	35 / 176 (19.89%)	29 / 221 (13.12%)	
occurrences (all)	58	39	
Oral Herpes			
subjects affected / exposed	2 / 176 (1.14%)	2 / 221 (0.90%)	
occurrences (all)	5	3	
Pharyngitis			
subjects affected / exposed	10 / 176 (5.68%)	7 / 221 (3.17%)	
occurrences (all)	10	7	
Sinusitis			
subjects affected / exposed	5 / 176 (2.84%)	2 / 221 (0.90%)	
occurrences (all)	8	2	
Rhinitis			
subjects affected / exposed	6 / 176 (3.41%)	4 / 221 (1.81%)	
occurrences (all)	7	5	
Tonsillitis			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	5	2	
Tooth Abscess			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	7	3	

Upper Respiratory Tract Infection			
subjects affected / exposed	8 / 176 (4.55%)	4 / 221 (1.81%)	
occurrences (all)	8	4	
Urinary Tract Infection			
subjects affected / exposed	5 / 176 (2.84%)	4 / 221 (1.81%)	
occurrences (all)	12	7	
Vaginal Infection			
subjects affected / exposed	0 / 176 (0.00%)	0 / 221 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Folate Deficiency			
subjects affected / exposed	5 / 176 (2.84%)	5 / 221 (2.26%)	
occurrences (all)	5	5	
Hypokalaemia			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Hypophosphataemia			
subjects affected / exposed	1 / 176 (0.57%)	1 / 221 (0.45%)	
occurrences (all)	1	1	
Iron Deficiency			
subjects affected / exposed	2 / 176 (1.14%)	3 / 221 (1.36%)	
occurrences (all)	2	3	
Vitamin B12 Deficiency			
subjects affected / exposed	4 / 176 (2.27%)	2 / 221 (0.90%)	
occurrences (all)	4	2	
Vitamin D Deficiency			
subjects affected / exposed	7 / 176 (3.98%)	6 / 221 (2.71%)	
occurrences (all)	7	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2017	To redefine the treatment target according to more stringent Crohn's Disease Activity Index (CDAI) and biomarker criteria as recommended by the study steering committee and considered scientifically more valid in the context of a treat to target strategy.
13 September 2017	To redefine the treatment target for subjects who did not have elevated C-reactive protein (CRP) at baseline.
23 November 2017	To extend study treatment to Week 104, to explore the effectiveness of longer-term ustekinumab treatment, and to explore de-escalation of ustekinumab dosing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study was limited by open-label design and randomisation of CDAI-70 responders at Week 16 only, that partly explain high Week 48 response rates.

Notes: