Clinical trial results:
Loss of RESponse to Ustekinumab treated by dose Escalation

Summary

EudraCT number	2018-004269-14
Trial protocol	BE
Global end of trial date	25 September 2024

Results information

Result version number	v2 (current)
This version publication date	25 June 2026
First version publication date	05 April 2026
Version creation reason	• Correction of full data set Update required in statistical tests.

Trial information

Trial identification

Sponsor protocol code	BIRD2018001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04245215
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Belgian IBD Research and Development (BIRD)
Sponsor organisation address	Leuvensesteenweg 643, Zaventem, Belgium, 1930
Public contact	Chief operating officer, Belgian IBD Research and Development (BIRD), 0032 499317005, ingrid.arijs@birdgroup.be
Scientific contact	Chief operating officer, Belgian IBD Research and Development (BIRD), 0032 499317005, ingrid.arijs@birdgroup.be

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	25 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 September 2024
Global end of trial reached?	Yes
Global end of trial date	25 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the clinical effect of ustekinumab re-induction ≈6mg/kg intravenously (IV) followed by either 90 mg subcutaneous (SC) ustekinumab every 8 weeks (q8w) or 90 mg SC ustekinumab every 4 weeks (q4w) in patients with Crohn's Disease who show a secondary loss of response over time

Protection of trial subjects:

This clinical trial was conducted in compliance with the principles of the Declaration of Helsinki (2008), the principles of Good Clinical Practice, and in accordance with all applicable regulatory requirements. The study was conducted on the basis of prior informed consent by the subjects to participate in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 108
Worldwide total number of subjects	108
EEA total number of subjects	108

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)	102

From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between February 2020 and October 2023 a total of 132 patients were screened and 108 patients were randomized.
First Patient In (FPI) was on 11Mar2020.
Last Patient In (LPI) was on 17Oct2023.
Last Patient Out (LPO) was on 25Sep2024.

Pre-assignment

Screening details:

Eligible Crohn's Disease patients were treated with ustekinumab at a standard maintenance dose of 90 mg every 8 weeks SC. Patients needed to have a documented primary response to standard IV induction with ustekinumab and a documented secondary loss of response based on Patient-Reported Outcomes and objective documentation of disease activity.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ustekinumab q4w

Arm description:

Subjects received a re-induction at baseline, with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. At week 4, the subjects in the q4w arm received the first blinded 90 mg SC injection of ustekinumab. Subsequently, subjects in the q4w arm received commercial available q8w ustekinumab (90 mg SC syringe at week 8, 16, 24, 32, 40, 48) alternated with q8w double blinded active ustekinumab (at week 12, 20, 28, 36, 44).

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

Dosage and administration details:

Subjects received subcutaneous ustekinumab 90 mg at week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44 and 48.

Investigational medicinal product name	ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a re-induction at baseline (Week 0), with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. Subjects with body weight ≤55 kg at Week 0 received 260 mg IV ustekinumab. Those subjects with body weight >55 kg and ≤85 kg received 390 mg IV ustekinumab. Subjects with body weight >85 kg at Week 0 received 520 mg IV ustekinumab.

Arm title	ustekinumab q8w

Arm description:

Subjects received a re-induction at baseline, with intravenous ustekinumab, in line with the EU SmPC,

on a weight-tiered basis at a dose of approximately 6 mg/kg. At week 4, the subjects in the q8w arm received the first blinded placebo injection. Subsequently, subjects in the q8w arm received commercial available q8w ustekinumab (90 mg SC syringe at week 8, 16, 24, 32, 40, 48) alternated with q8w double blinded placebo (at week 12, 20, 28, 36, 44).

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a re-induction at baseline (Week 0), with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. Subjects with body weight ≤55 kg at Week 0 received 260 mg IV ustekinumab. Those subjects with body weight >55 kg and ≤85 kg received 390 mg IV ustekinumab. Subjects with body weight >85 kg at Week 0 received 520 mg IV ustekinumab.

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

Dosage and administration details:

Subjects received subcutaneous ustekinumab 90 mg at week 8, 16, 24, 32, 40 and 48.

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

Dosage and administration details:

Subjects received subcutaneous placebo at week 4, 12, 20, 28, 36 and 44.

Number of subjects in period 1	ustekinumab q4w	ustekinumab q8w
Started	54	54
Completed	37	35
Not completed	17	19
Consent withdrawn by subject	1	3
Adverse event, non-fatal	-	1
Pregnancy	-	1
Patient non-compliance	1	-
Disease exacerbation	12	10
Lack of efficacy	3	4

Baseline characteristics

Reporting groups	
Reporting group title	ustekinumab q4w
Reporting group description:	
Subjects received a re-induction at baseline, with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. At week 4, the subjects in the q4w arm received the first blinded 90 mg SC injection of ustekinumab. Subsequently, subjects in the q4w arm received commercial available q8w ustekinumab (90 mg SC syringe at week 8, 16, 24, 32, 40, 48) alternated with q8w double blinded active ustekinumab (at week 12, 20, 28, 36, 44).	
Reporting group title	ustekinumab q8w
Reporting group description:	
Subjects received a re-induction at baseline, with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. At week 4, the subjects in the q8w arm received the first blinded placebo injection. Subsequently, subjects in the q8w arm received commercial available q8w ustekinumab (90 mg SC syringe at week 8, 16, 24, 32, 40, 48) alternated with q8w double blinded placebo (at week 12, 20, 28, 36, 44).	

Reporting group values	ustekinumab q4w	ustekinumab q8w	Total
Number of subjects	54	54	108
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	52	50	102
From 65-84 years	2	4	6
85 years and over	0	0	0
Age continuous Units: years			
median	41	40	
inter-quartile range (Q1-Q3)	32 to 57	32 to 53	-
Gender categorical Units: Subjects			
Female	35	32	67
Male	19	22	41

End points

End points reporting groups

Reporting group title	ustekinumab q4w

Reporting group description:

Subjects received a re-induction at baseline, with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. At week 4, the subjects in the q4w arm received the first blinded 90 mg SC injection of ustekinumab. Subsequently, subjects in the q4w arm received commercial available q8w ustekinumab (90 mg SC syringe at week 8, 16, 24, 32, 40, 48) alternated with q8w double blinded active ustekinumab (at week 12, 20, 28, 36, 44).

Reporting group title	ustekinumab q8w

Reporting group description:

Subjects received a re-induction at baseline, with intravenous ustekinumab, in line with the EU SmPC, on a weight-tiered basis at a dose of approximately 6 mg/kg. At week 4, the subjects in the q8w arm received the first blinded placebo injection. Subsequently, subjects in the q8w arm received commercial available q8w ustekinumab (90 mg SC syringe at week 8, 16, 24, 32, 40, 48) alternated with q8w double blinded placebo (at week 12, 20, 28, 36, 44).

Primary: Proportion of patients with steroid free clinical remission (PRO-2 remission: AP ≤ 1 AND SF ≤ 3) and FCP <250µg/g at week 48

End point title	Proportion of patients with steroid free clinical remission (PRO-2 remission: AP ≤ 1 AND SF ≤ 3) and FCP <250µg/g at week 48

End point description:

PRO : Patient Reported Outcomes
AP : Abdominal Pain : average scoring for abdominal pain for 7 days (0=none; 1=mild, 2=moderate; 3= severe)
SF : Stool Frequency : average number of liquid/very soft stools for 7 days
FCP : Fecal Calprotectin

End point type	Primary

End point timeframe:

Week 48

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	54		
Units: subjects				
steroid free clinical remission	8	10		

Statistical analyses

Statistical analysis title	Primary endpoint analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	0.0502
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09487
upper limit	0.1953

Secondary: Proportion of patients with complete endoscopic remission (SES-CD <3) at week 48

End point title	Proportion of patients with complete endoscopic remission (SES-CD <3) at week 48
End point description:	
SES-CD : simple endoscopic score for Crohn's Disease	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	50		
Units: subjects	4	3		

Statistical analyses

Statistical analysis title	Complete endoscopic remission analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.787
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.164
upper limit	3.792

Secondary: Proportion of patients with endoscopic remission (SES-CD <5) at week 48

End point title	Proportion of patients with endoscopic remission (SES-CD <5) at week 48
End point description:	
SES-CD : simple endoscopic score for Crohn's Disease	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	50		
Units: subjects	15	8		

Statistical analyses

Statistical analysis title	endoscopic remission analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.467
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.178
upper limit	1.223

Secondary: Proportion of patients with endoscopic response (≥50% decrease in SES-CD) at week 48

End point title	Proportion of patients with endoscopic response (≥50% decrease in SES-CD) at week 48
End point description:	
SES-CD : simple endoscopic score for Crohn's Disease	
End point type	Secondary

End point timeframe:

Week 48

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	50		
Units: subjects	12	8		

Statistical analyses

Statistical analysis title	endoscopic response analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.837
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	2.187

Secondary: Proportion of patients with clinical remission (PRO-2 remission: AP ≤ 1 AND SF ≤ 3) at week 8 after IV re-induction

End point title	Proportion of patients with clinical remission (PRO-2 remission: AP ≤ 1 AND SF ≤ 3) at week 8 after IV re-induction

End point description:

PRO : Patient Reported Outcomes
AP : Abdominal Pain : average scoring for abdominal pain for 7 days (0=none; 1=mild, 2=moderate; 3= severe)
SF : Stool Frequency : average number of liquid/very soft stools for 7 days

End point type	Secondary

End point timeframe:

Week 8

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: subjects	19	21		

Statistical analyses

Statistical analysis title	clinical remission week 8 analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.143
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.526
upper limit	2.484

Secondary: Proportion of patients with clinical remission (PRO-2 remission: AP ≤ 1 AND SF ≤ 3) at week 48

End point title	Proportion of patients with clinical remission (PRO-2 remission: AP ≤ 1 AND SF ≤ 3) at week 48

End point description:

PRO : Patient Reported Outcomes
AP : Abdominal Pain : average scoring for abdominal pain for 7 days (0=none; 1=mild, 2=moderate; 3= severe)
SF : Stool Frequency : average number of liquid/very soft stools for 7 days

End point type	Secondary

End point timeframe:

Week 48

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	50		
Units: subjects	16	18		

Statistical analyses

Statistical analysis title	clinical remission week 48 analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.278
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.562
upper limit	2.904

Secondary: Proportion of patients with biomarker remission (CRP <5 mg/L and FCP <250 µg/g) at week 48

End point title	Proportion of patients with biomarker remission (CRP <5 mg/L and FCP <250 µg/g) at week 48
End point description: CRP : C-reactive protein FCP : Fecal calprotectin	
End point type	Secondary
End point timeframe: Week 48	

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: subjects	18	13		

Statistical analyses

Statistical analysis title	biomarker remission analysis
Comparison groups	ustekinumab q4w v ustekinumab q8w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.63

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.268
upper limit	1.483

Secondary: Proportion of Patients With Serious Adverse Events at Week 48

End point title	Proportion of Patients With Serious Adverse Events at Week 48

End point description:

End point type	Secondary

End point timeframe:

week 48

End point values	ustekinumab q4w	ustekinumab q8w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	54		
Units: subjects	9	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signature of informed consent form up to week 48 in the study. For SAE's up to 60 days after the last study treatment.

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	q4w arm
Reporting group description: -	
Reporting group title	q8w arm

Reporting group description: -

Serious adverse events	q4w arm	q8w arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 54 (16.67%)	7 / 54 (12.96%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Abdominal pain after right hemicolectomy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac ablation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laparoscopic right hemicolectomy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Extensive colitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastro-enteritis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small bowel ileus			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
(sub) Obstruction			
subjects affected / exposed	3 / 54 (5.56%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowel obstruction terminal ileitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presacral abscess			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stricturing Crohn's Disease			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flare of Crohn's Disease			

subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenosis hepaticojejunostomia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Stress fracture femoral neck left			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia due to Infliximab			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Recurrent abdominal wall hernia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection Giardia Lamblia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
E. Coli urosepsis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Electrolyte abnormalities			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	q4w arm	q8w arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 54 (81.48%)	46 / 54 (85.19%)	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 54 (9.26%)	7 / 54 (12.96%)	
occurrences (all)	8	8	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 54 (14.81%)	5 / 54 (9.26%)	
occurrences (all)	8	5	
Gastrointestinal disorders			
gastro-enteritis			
subjects affected / exposed	4 / 54 (7.41%)	4 / 54 (7.41%)	
occurrences (all)	4	5	
Worsening of Crohn's Disease			
subjects affected / exposed	6 / 54 (11.11%)	4 / 54 (7.41%)	
occurrences (all)	6	5	
Abdominal pain			
subjects affected / exposed	10 / 54 (18.52%)	13 / 54 (24.07%)	
occurrences (all)	11	14	
Skin and subcutaneous tissue disorders			
Skin abnormalities			
subjects affected / exposed	6 / 54 (11.11%)	9 / 54 (16.67%)	
occurrences (all)	6	11	
Psychiatric disorders			
Psychiatric symptoms			
subjects affected / exposed	5 / 54 (9.26%)	3 / 54 (5.56%)	
occurrences (all)	7	5	

Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	18 / 54 (33.33%)	22 / 54 (40.74%)	
occurrences (all)	24	42	
Infections and infestations			
Respiratory infection			
subjects affected / exposed	21 / 54 (38.89%)	25 / 54 (46.30%)	
occurrences (all)	35	32	
Flu			
subjects affected / exposed	7 / 54 (12.96%)	8 / 54 (14.81%)	
occurrences (all)	9	9	
Metabolism and nutrition disorders			
Lab abnormalities/deficiencies			
subjects affected / exposed	10 / 54 (18.52%)	15 / 54 (27.78%)	
occurrences (all)	12	22	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2020	Modifications regarding inclusion criteria (less strict), addition of 'window' regarding IV re-induction of ustekinumab and patient visits, update of the timelines for the study.
17 December 2020	Modifications regarding inclusion criteria (to ensure that included patients have at least inflammation in the gut if loss of response was based on the increase in biomarker(s)) and exclusion criteria (clarification), update of study timelines, removal of collection of additional stool samples for substudy.
01 April 2022	Modification in one of the inclusion criteria (to ensure patients with primary response at week 20 instead of week 16 are not screenfailed), modification regarding the visit window for the screening endoscopy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/41747777