Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Study Evaluating the Safety and Efficacy of Guselkumab for the Treatment of Participants with Crohn's Disease After Surgical Resection

Summary

EudraCT number	2022-002389-33
Trial protocol	FR IT ES HU BE
Global end of trial date	10 October 2023

Results information

Result version number	v1 (current)
This version publication date	06 October 2024
First version publication date	06 October 2024

Trial information

Trial identification

Sponsor protocol code	CNTO1959CRD3007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05784129
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Pharmaceuticals, Inc
Sponsor organisation address	800 Ridgeview Drive, Horsham PA, United States, 19044
Public contact	Clinical Registry Group, Janssen Pharmaceuticals, Inc, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Pharmaceuticals, Inc, 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	10 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy and safety of subcutaneous guselkumab treatment versus placebo in reducing the recurrence of Crohn's disease (CD) in adult patients who have recently undergone a surgical resection for Crohn's disease.

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	21 February 2023
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	United States: 4
Worldwide total number of subjects	4
EEA total number of subjects	0

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)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Due to early termination of the study, treatment period was up to Week 16 only. Subjects were followed up for safety analysis till Week 28. The planned efficacy analysis was not performed due to the early study termination for reasons unrelated to safety or efficacy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Guselkumab 200 mg + Guselkumab 100 mg

Arm description:

Subjects were assigned to receive guselkumab 200 milligrams (mg) subcutaneous (SC) injection at Week 0 followed by guselkumab 100 mg SC injection at every 8 weeks thereafter until study termination (i.e., up to Week 16).

Arm type	Experimental
Investigational medicinal product name	Guselkumab
Investigational medicinal product code	CNTO1959
Other name	Tremfya
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received guselkumab 200 mg at Week 0 and 100 mg at Weeks 8, and 16.

Arm title	Placebo matched to Guselkumab

Arm description:

Subjects were assigned to receive placebo matched to guselkumab SC injections at week 0 and at every 8 weeks thereafter until study termination (i.e., up to Week 16).

Arm type	Experimental
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 placebo matched to guselkumab at Weeks 0, 8, and 16.

Number of subjects in period 1	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab
Started	2	2
Treated at Weeks 0, 8 and 16	1	2
Treated at Weeks 0 and 8	1	0
Completed	0	0
Not completed	2	2
Study terminated by sponsor	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Guselkumab 200 mg + Guselkumab 100 mg
Reporting group description:	
Subjects were assigned to receive guselkumab 200 milligrams (mg) subcutaneous (SC) injection at Week 0 followed by guselkumab 100 mg SC injection at every 8 weeks thereafter until study termination (i.e., up to Week 16).	
Reporting group title	Placebo matched to Guselkumab
Reporting group description:	
Subjects were assigned to receive placebo matched to guselkumab SC injections at week 0 and at every 8 weeks thereafter until study termination (i.e., up to Week 16).	

Reporting group values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab	Total
Number of subjects	2	2	4
Title for AgeCategorical Units: subjects			
Title for AgeContinuous			
Here, "0.99999" indicated that no data is reported for age continuous in order to protect and maintain subject privacy/confidentiality.			
Units: years			
arithmetic mean	0.99999	0.99999	
standard deviation	± 0.99999	± 0.99999	-
Title for Gender Units: subjects			
Female	0	0	0
Male	0	0	0
Not reported	2	2	4

End points

End points reporting groups

Reporting group title	Guselkumab 200 mg + Guselkumab 100 mg

Reporting group description:

Subjects were assigned to receive guselkumab 200 milligrams (mg) subcutaneous (SC) injection at Week 0 followed by guselkumab 100 mg SC injection at every 8 weeks thereafter until study termination (i.e., up to Week 16).

Reporting group title	Placebo matched to Guselkumab

Reporting group description:

Subjects were assigned to receive placebo matched to guselkumab SC injections at week 0 and at every 8 weeks thereafter until study termination (i.e., up to Week 16).

Primary: Percentage of Subjects with Endoscopic Recurrence Prior to or at Week 48

End point title	Percentage of Subjects with Endoscopic Recurrence Prior to or at Week 48[1]

End point description:

Endoscopic recurrence was defined by modified Rutgeerts score greater than or equal to (>=) i2a in neo-terminal ileum, anastomotic site, or its equivalent in gastrointestinal (GI) tract (e.g., colonic ulceration). The modified Rutgeerts score ranged from i0 to i4, where i0 (No lesions), i1 (less than [<] 5 aphthous lesions), i2 (greater than [>] 5 aphthous lesions with normal mucosa between lesions or skip areas of larger lesions or lesions confined to ileocolonic anastomosis [<1 centimeter (cm) in length]), i2a (lesions confined to ileocolonic anastomosis [including anastomotic stenosis]), i2b (more than 5 aphthous ulcers or larger lesions, with normal mucosa in-between, in the neoterminal ileum [with or without anastomotic lesions]), i3 (diffuse aphthous ileitis with diffusely inflamed mucosa), i4 (large ulcers with diffuse mucosal inflammation or nodules or stenosis in neoterminal ileum). Higher score indicated worsening.

End point type	Primary

End point timeframe:

Baseline (Day 1) up to Week 48

Notes:

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

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[2] - No subject was available due to early termination.

[3] - No subject was available due to early termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Remission Without Disease Recurrence at Week 48

End point title	Percentage of Subjects with Clinical Remission Without Disease

	Recurrence at Week 48

End point description:

Clinical remission without disease recurrence at Week 48 was a composite endpoint defined by (1) Crohn’s disease activity index (CDAI) score <150 at Week 48 & (2) no endoscopic recurrence with Rutgeerts score <i2a by Week 48 & (3) no experienced disease recurrence. Disease recurrence: (1) >=70 point increase from baseline CDAI at >8 weeks after randomization & CDAI >=200 and evidence of endoscopic recurrence or (2) initiation of physician-prescribed corticosteroids or increasing steroid dose of >5 mg/day for CD and endoscopic recurrence or (3) new draining or reopening of an internal or external fistula or (4) new perianal abscess or (5) new intra-abdominal abscess more than 3 months post index surgery. If patient tested positive for enteric pathogen, infection should be treated and then subject should be reassessed whether they meet disease recurrence. Due to early termination of study, no formal data collection & analysis was possible & thus no data was collected for this endpoint.

End point type	Secondary

End point timeframe:

At Week 48

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[4] - No formal analysis was performed due to early termination of study.

[5] - No formal analysis was performed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Recurrence

End point title	Time to Disease Recurrence

End point description:

Disease recurrence was defined as (1) >=70 point increase from baseline in CDAI score at >8 weeks after randomization & CDAI score >=200 and evidence of endoscopic recurrence with Rutgeerts score <i2a or (2) initiation of physician-prescribed corticosteroids or increase in steroid dose of >5 mg/day for treatment of CD and endoscopic recurrence or (3) new draining or reopening of an internal or external fistula or (4) new perianal abscess or (5) new intra-abdominal abscess more than 3 months post index surgery. If a patient had a positive test for enteric pathogen, infection should be treated and then subject should be reassessed for whether they meet disease recurrence. Due to early termination of the study, no formal data collection and analysis was possible and thus no data was collected for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to Week 48

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: weeks				
median (full range (min-max))	(to)	(to)		

Notes:

[6] - No formal analysis was performed due to early termination of study.

[7] - No formal analysis was performed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with No Abdominal Pain at Week 48

End point title	Percentage of Subjects with No Abdominal Pain at Week 48

End point description:

Abdominal pain free at Week 48 was defined as abdominal pain (AP) score = 0 at Week 48. The scoring was done on a 4-point scale, ranged from 0 to 3, where 0 =none, 1=mild pain, 2 =moderate pain and 3 =severe pain. Higher score indicated severe pain. Due to early termination of the study, no formal data collection and analysis was possible and thus no data was collected for this endpoint.

End point type	Secondary

End point timeframe:

At Week 48

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[8] - No formal analysis was performed due to early termination of study.

[9] - No formal analysis was performed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point description:

Number of subjects with TEAEs and TESAEs were reported. An adverse event (AE) was any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. A SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant

disability/incapacity; congenital anomaly. Any AE/SAE occurring at or after the initial administration of study intervention through early termination of trial (up to Week 28) was considered to be treatment emergent. Safety analysis set included all randomised subjects who received at least 1 dose of study intervention and were analysed according to the study intervention they actually received.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to 12 weeks after last study dose administration (up to Week 28)

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: subjects				
Subjects with TEAEs	1	1		
Subjects with TESAEs	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Recurrence of Symptoms

End point title	Time To Recurrence of Symptoms

End point description:

Time-to-recurrence of symptoms was defined as time to attaining an AP mean daily score >1 (and also >1 point higher than baseline) along with stool frequency (SF) mean daily score >3 (and also >3 higher per day than baseline) for 2 consecutive weeks through Week 48. AP score scale was done on a 4-point scale, ranged from 0 to 3, where 0 =none, 1=mild pain, 2 =moderate pain and 3 =severe pain. Higher score indicated severe pain. SF score was calculated from the total number of liquid or very soft stools in the previous 7 days. Due to early termination of the study, no formal data collection and analysis was possible and thus no data was collected for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to Week 48

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: weeks				
median (full range (min-max))	(to)	(to)		

Notes:

[10] - No formal analysis was performed due to early termination of study.

[11] - No formal analysis was performed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Guselkumab Concentrations Over Time

End point title	Serum Guselkumab Concentrations Over Time[12]

End point description:

Serum guselkumab concentrations over time were reported. Pharmacokinetic (PK) analysis set included all randomised subjects who received at least 1 dose of study intervention, and had at least one valid blood sample drawn postbaseline for PK analysis and were analysed according to the study intervention they actually received. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number analysed) signifies number of subjects analysed at specified categories. No summary analysis was done as study was terminated early and subject wise data were reported. This endpoint was planned to be analysed for "Guselkumab 200 mg + Guselkumab 100 mg" arm only.

End point type	Secondary

End point timeframe:

At Weeks 0, 8, 16

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for "Guselkumab 200 mg + Guselkumab 100 mg" arm only.

End point values	Guselkumab 200 mg + Guselkumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: micrograms/millilitres (mcg/mL)				
number (not applicable)				
Subject 1 (Week 0)	0			
Subject 1 (Week 8)	1.68920			
Subject 1 (Week 16)	0.70957			
Subject 2 (Week 0)	0			
Subject 2 (Week 8)	2.87917			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Steroid Free Clinical Remission at Week 48

End point title	Percentage of Subjects with Steroid Free Clinical Remission at Week 48

End point description:

Steroid free clinical remission at Week 48 is defined as CDAI score <150 and no corticosteroids within 30 days. The CDAI score was a validated multi-item measure of severity of illness derived as a weighted sum of 8 different CD-related variables. The CDAI score was assessed by collecting information on 8 different Crohn's disease-related variables: extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s), and/or opiates, and general well-being. The last 4 variables were scored over 7 days by the subject on a diary card. In general, CDAI score ranges from 0 to approximately 600; higher score indicated higher disease activities. Due to early termination of the study, no formal data collection and analysis was possible and thus no data was collected for this endpoint.

End point type	Secondary

End point timeframe:

At Week 48

End point values	Guselkumab 200 mg + Guselkumab 100 mg	Placebo matched to Guselkumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	0[14]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[13] - No formal analysis was performed due to early termination of study.

[14] - No formal analysis was performed due to early termination of study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Baseline (Day 1) up to 12 weeks after last study dose administration (up to Week 28)

Adverse event reporting additional description:

Safety analysis set included all randomised subjects who received at least 1 dose of study intervention and were analysed according to the study intervention they actually received.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo matched to Guselkumab (Experimental)

Reporting group description:

Subjects were assigned to receive placebo matched to guselkumab SC injections at week 0 and at every 8 weeks thereafter until study termination (i.e., up to Week 16).

Reporting group title	Guselkumab 200 mg + Guselkumab 100 mg

Reporting group description:

Subjects were assigned to receive guselkumab 200 milligrams (mg) subcutaneous (SC) injection at Week 0 followed by guselkumab 100 mg SC injection at every 8 weeks thereafter until study termination (i.e., up to Week 16).

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Non SAEs are reported only when at least one non SAE occurred in the subjects.

Serious adverse events	Placebo matched to Guselkumab (Experimental)	Guselkumab 200 mg + Guselkumab 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Campylobacter Gastroenteritis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo matched to Guselkumab (Experimental)	Guselkumab 200 mg + Guselkumab 100 mg	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2022	The purpose of this amendment was to further clarify how cross over to open-label guselkumab treatment for subjects was handled, which included the addition of a separate Schedule of Activities for subjects who cross over to guselkumab.

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.

Due to early termination of study, protocol planned primary endpoint and few of secondary endpoints were not evaluable. Termination was not related to safety or efficacy of guselkumab.

Notes: