A Phase 3, Randomized, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Efficacy and Safety of Guselkumab in Participants with Fistulizing, Perianal Crohn*s Disease

Published: 01-06-2022
Last updated: 14-12-2024

This study has been transitioned to CTIS with ID 2023-504740-33-00 check the CTIS register for the current data. Objectives• To evaluate the clinical efficacy of guselkumab in fistulizing, perianal Crohn*s disease• To assess the overall safety of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON53768

Source
ToetsingOnline

Brief title
FUZION

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn, inflammatory bowel disease (IBD)

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: Crohn's Disease, Guselkumab, Phase 3, Placebo-controlled

Outcome measures

Primary outcome

The primary endpoint of this study is the proportion of participants who

achieve combined fistula remission at Week 2.

Secondary outcome

-proportion of participants who achieve combined fistula remission at week 48

-proportion of participants who achieve clinically assessed fistula remission

at week 24

-proportion of participants who achieve radiological fistula remission based on

radiological findings assessed by MRI at week 24

-proportion of participants who achieve clinically assessed fistula response at

week 24

-proportion of participants who achieve clinically assessed fistula response at

week 12

Study description

Background summary

Guselkumab (TREMFYA®) is a fully human immunoglobulin G1 lambda (IgG1 *) monoclonal antibody (mAb) that binds to the p19 subunit of human interleukin (IL)-23 with high specificity and affinity. Binding of guselkumab to the

IL-23p19 subunit blocks the subsequent binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23 specific intracellular signaling and subsequent activation and cytokine production. Guselkumab inhibits the biological activity of IL-23 in all in vitro assays examined. A rapidly growing body of evidence suggests that dysregulated IL 23/IL-17 responses contribute to chronic inflammation underlying the pathophysiology of many immune-mediated diseases, including psoriasis, multiple sclerosis, rheumatoid arthritis, and inflammatory bowel disease.

Study objective

This study has been transitioned to CTIS with ID 2023-504740-33-00 check the CTIS register for the current data.

Objectives
• To evaluate the clinical efficacy of guselkumab in fistulizing, perianal Crohn*s disease
• To assess the overall safety of guselkumab
Primary Endpoint
The primary endpoint of this study is the proportion of participants who achieve combined fistula
remission at Week 24
* Combined fistula remission is defined as 100% closure of all treated external openings
without development of new fistulas or abscesses and without any drainage by the external openings [occurring spontaneously or after gentle finger compression] and
absence of collections >2 cm of the perianal fistulas, confirmed by a blinded central
review of the MRI results.
Major Secondary Endpoints
• Proportion of participants who achieve combined fistula remission at Week 48
• Proportion of participants who achieve clinically assessed fistula remission at Week 24
* Clinically assessed fistula remission is defined as 100% closure of all treated external openings, without development of new fistulas or abscesses and without any drainage by
the external openings, occurring spontaneously or after gentle finger compression
• Proportion of participants who achieve radiological fistula remission based on radiological findings assessed by MRI at Week 24
* Radiological remission is defined as absence of collections >2 cm of the perianal fistulas,
confirmed by a blinded central review of the MRI results
• Proportion of participants who achieve clinically assessed fistula response at Week 24
* Clinically assessed fistula response is defined as closure of at least 50% of

all external
openings that were draining at baseline
• Proportion of participants who achieve clinically assessed fistula response at Week 12

Secondary Endpoints Related to Crohn*s Disease: Clinical Measures
• Change from baseline in Crohn's Disease Activity Index (CDAI) by visit over time through Week 48
• Proportion of participants who achieve clinical remission (CDAI <150) by visit over time through Week 48 among participants with CDAI >150 at baseline
• Proportion of participants who achieve a clinical response (>=100-point reduction from baseline in CDAI, or CDAI <150) by visit over time through Week 48 among participants with CDAI >150 at baseline
• Proportion of participants who achieve steroid-free clinical remission defined as CDAI <150 and not receiving corticosteroids by visit over time through Week 48 among participants with CDAI >150 at baseline
• Proportion of participants who achieve combined clinical response and clinically assessed fistula response among participants with CDAI > 220 at baseline at Week 24 and Week 48
• Proportion of participants who achieve combined clinical response and clinically assessed fistula remission among participants with CDAI > 220 at baseline at Week 24 and Week 48
• Proportion of participants who achieve combined clinical remission and clinically assessed fistula remission among participants with CDAI > 220 at baseline at Week 24 and Week 48
• Proportion of participants who achieve combined clinical remission and clinically assessed fistula response among participants with CDAI > 220 at baseline at Week 24 and Week 48
• Proportion of participants who achieve combined clinical response and clinically assessed fistula response at Week 24 and Week 48
• Proportion of participants who achieve combined clinical response and clinically assessed fistula remission at Week 24 and Week 48
• Proportion of participants who achieve combined clinical remission and clinically assessed fistula response at Week 24 and Week 48
• Proportion of participants who achieve combined clinical remission and clinically assessed fistula remission at Week 24 and Week 48

Secondary Endpoints Related to Fistula: Physical Assessment
• Changes from baseline in Perianal Disease Activity Index (PDAI) overall score, discharge score, and pain score by visit over time through Week 48
• Proportion of participants who achieve clinically assessed fistula response by visit over time through Week 48
• Proportion of participants who achieve clinically assessed fistula remission by visit over time through Week 48
• Proportion of participants who achieve clinically assessed fistula remission at Week 48 among the participants who achieve clinical fistula remission at Week 24

• Proportion of participants achieving clinically assessed fistula remission at Week 48 among those who achieve fistula remission or response (defined either by clinical or radiological assessment) at Week 24
• Time to clinical fistula remission
Secondary Endpoints Related to Fistula: Radiological Assessment Confirmed by Blinded
Central Review
• Proportion of participants who achieve radiological fistula predominantly fibrotic status for all existent fistulas assessed by MRI at Week 24
• Proportion of participants who achieve radiological fistula predominantly fibrotic status for all existent fistulas assessed by MRI at Week 48
• Proportion of participants who achieve radiological remission based on radiological findings assessed by MRI at Week 48
• Proportion of participants who achieve radiological remission assessed by MRI at Week 48 among the participants who achieve radiological remission at Week 24
• Proportion of participants who achieve combined clinically assessed and radiological (assessed by MRI) fistula remission at Week 48 among the participants who achieve combined clinical and radiological fistula remission at Week 24
• Proportion of participants who achieve combined clinically assessed and radiological (assessed by MRI) fistula remission at Week 48 among the participants who achieve clinical fistula response at Week 24
• Proportion of participants with proctitis at Week 48 among participants with MRI-confirmed proctitis at baseline
• Change from baseline in magnetic resonance novel index for fistula imaging in Crohn*s disease (MAGNIFI-CD) by visit over time through Week 48

Secondary Endpoints Related to Patient-reported Outcomes
• Change from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) by visit over time through Week 48
• Change from baseline in evaluation of drug effectiveness from the participant*s perspective (patient-reported outcomes [PROs]), including, disease impact (Functional Assessment of Chronic Illness Therapy - fatigue [FACIT-fatigue]), and productivity (Work Productivity and Activity Impairment Questionnaire: Crohn*s Disease [WPAI:CD]) by visit over time through Week 48
• Change from baseline in quality-of-life (European Quality-of-Life Five Dimension Five Level Scale [EQ5D-5L]) by visit over time through Week 48
• Change from baseline in the Jorge-Wexner score by visit over time through Week 48
• Change from baseline in the Inflammatory Bowel Disease-Disability Index (IBD-DI) by visit over time through Week 48
Secondary Endpoints Related to Safety
• Number of participants with 1 or more treatment-emergent adverse events through Week 48 by Medical Dictionary for Regulatory Activities (MedDRA) system-organ class and preferred term.
• Number of participants with 1 of more treatment-emergent serious adverse events through Week 48 by MedDRA system-organ class and preferred term.

Please refer to the Statistical Analysis Plan (SAP) for the secondary endpoints related to the LTE up to Week 96.

Exploratory Endpoints
• Change from baseline in Van Assche scale by visit over time through Week 48
• Change from baseline in sexual function by visit over time through Week 48, based on Female Sexual Function Index (FSFI) and International Index of Erectile Function (IIEF)
• Proportion of participants who achieve fistula remission based on radiological findings ass

Study design

The FUZION study is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of guselkumab in participants aged >=18 years with fistulizing, perianal Crohn*s disease. Eligible participants must be diagnosed with Crohn*s disease (confirmed by clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical
investigations) for a minimum of 3 months, and must have at least one active draining perianal fistula confirmed by the screening MRI results, with or without a seton in place at screening. The result of the MRI at screening must be interpreted centrally to assess eligibility of participants; local review is permitted in case the central review is not available on time.

The study consists of a screening period of up to 6 weeks prior to baseline data collection, a 48-week randomized treatment phase with 3 treatment groups, and a post-intervention safety follow-up (as a site visit or telephone contact) occurring 16 weeks after the participant's last dose of study intervention (Week 64 ±7 days).

Please refer to Section 4.1.1 for details on the long-term extension (LTE) for participants who complete the 48-week treatment period and who, and in the opinion of the investigator, will continue to benefit from the study intervention.

The study intervention will be administered at the site by a health care professional up to Week 16. At Weeks 20, 28 and 44, at the discretion of the investigator and participant, and after appropriate and documented training, participants may self-administer study intervention at home. A caregiver may also be trained to administer study intervention. After receiving training at the Week 12 site visit, participants who are eligible for self- (or caregiver) administration of study intervention will be supplied with study intervention for at-home administration and will have their first at-home administration at Week 20.

Participants who are unable or unwilling to have study intervention

administered away from the study site will continue administration at the study site. The use of concomitant therapies used at baseline for fistulizing, perianal Crohn*s disease such as immunomodulators (ie, azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate [MTX]), oral corticosteroids, or procedures such as drainage, fistula
curettage and/or seton placement if clinically indicated, is permitted during the screening phase. Any antibiotic therapies initiated or ongoing during the screening phase must be stopped at baseline. Participants should not initiate or change any other concomitant Crohn*s disease-specific medical therapies, other than those permitted per the protocol. During the study period, efficacy, safety, PK, PD, immunogenicity, and biomarkers will be assessed per the Schedule of Activities. Key safety assessments will include adverse events (AEs), clinical laboratory tests (hematology and chemistry), vital signs, physical examination, screening electrocardiogram (ECG), monitoring for hypersensitivity reactions, injection-site reactions, and early detection of active tuberculosis (TB).
An Independent Data Monitoring Committee will be commissioned for this study.

Intervention

INTERVENTION GROUPS AND DURATION
Participants enrolled in the study will be randomized (2:2:1) to one of 3 treatment groups:
Group 1: A total of 112 participants will receive guselkumab 200 mg IV at Weeks 0, 4 and 8. At Week 12, participants will switch to guselkumab 200 mg SC q4w through to Week 48.
Group 2: A total of 112 participants will receive guselkumab 200 mg IV at Weeks 0, 4 and 8. At Week 16, participants will switch to guselkumab 100 mg SC q8w through to Week 48.
Group 3: A total of 56 participants will receive placebo IV at Weeks 0, 4 and 8. At Week 12, participants will switch to placebo SC q4w through to Week 20. At Week 24, the participants* fistula status will be clinically assessed, and participants receiving placebo will continue treatment in the study based on their clinically assessed fistula response status:
* Placebo responders: Continue placebo SC q4w from Week 24 through to Week 48.
* Placebo non-responders: Receive guselkumab 400 mg SC q4w from Week 24 through Week 32. At Week 36, participants will switch to guselkumab 200 mg SC q4w through to Week 48. Placebo non-responders will be analyzed as failures.
In addition, placebo administrations (IV and SC) will be given, as appropriate, to maintain the blind throughout the duration of the study. Clinically assessed fistula response is defined as a closure of at least 50% of all external openings that were draining at baseline. Participants in all treatment groups will be clinically assessed for their fistula response status at Week 24. No dose modifications are planned/permitted for participants in any of the study groups before assessment of the primary endpoint at Week 24. At Week 24, non-responders in the guselkumab or placebo groups may receive one blinded dose adjustment if considered as non-responders, and will be analyzed as failures.

Participants receiving guselkumab may receive one dose adjustment at Week 24 as follows:
* Participants randomized to Group 1 (guselkumab 200 mg SC q4w) may receive a sham dose optimization.
* Participants randomized to Group 2 (guselkumab 100 mg SC q8w) may switch to guselkumab 200 mg SC q4w.

Long-term Extension up to Week 96
The LTE will be conducted approximately from Week 48 through Week 96.
At the Week 48 time-point, participants who complete the 48-week treatment period and who, and in the opinion of the investigator, will continue to benefit from the study intervention (ie, based on Week 48 clinical evaluations), may be eligible to enter the LTE. During the LTE, participants will
continue to receive the blinded study intervention in the LTE until study unblinding, which will occur after the Week 48 database lock (DBL).
Upon study unblinding after the Week 48 DBL, participants receiving placebo will be discontinued from study intervention and will complete a SFU visit at that time-point. Participants receiving guselkumab will continue to receive their assigned regimens for the remaining duration of the LTE
through Week 96. The SFU visit of the LTE will occur at approximately Week 112 (ie, approximately 16 weeks after their last study intervention administration at Week 96).

Study burden and risks

SAFETY EVALUATIONS
Safety evaluations conducted at each study visit will include the assessment of AEs, at the visit and those occurring between evaluation visits, a tuberculosis evaluation and other infection assessments, clinical laboratory blood tests (complete blood count and serum chemistries), vital signs, suicidality assessment, concomitant medication review, and observations for injection-site reactions, reactions temporally associated with an infusion, and/or allergic reactions.

Contacts

Public
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
BE
Scientific

Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Aged 18 years (or the legal age of consent in the jurisdiction in which the study is taking
place) or over.
2. Must have a diagnosis of Crohn*s disease with a minimum duration of at least 3 months
(confirmed by clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical investigations).
3. Has at least one active draining perianal fistula as a complication of Crohn*s disease,
confirmed by screening MRI results.
4.2 Is naïve to biologics, or has previously demonstrated lack of initial response (ie, primary
non-responders), responded initially but then lost response with continued therapy (ie,
secondary non-responders), or were intolerant to a maximum of 2 classes of biologic
agents at a dose approved for the treatment of Crohn's disease (ie, infliximab, adalimumab, certolizumab pegol, vedolizumab, or approved biosimilars for these agents). Please refer to Appendix 4 for details.
OR
History of failure to respond to, or tolerate, at least 1 of the following therapies for the

treatment of Crohn's disease: oral corticosteroids (including budesonide and beclomethasone dipropionate) or immunomodulators (AZA, 6-MP, MTX).
Participants with prior exposure to IL-12/23 or IL-23 agents are ineligible for entry into
this protocol, with the exception of participants who have had exposure to ustekinumab
at its approved labeled dosage AND have met the required 16 week washout criterion
AND have not demonstrated failure or intolerance to ustekinumab. Please refer to Appendix 5 for details.
5.1 Had a history of failure to respond to, or tolerate, at least 1 of the following therapies
for fistula treatment: antibiotics (ie, ciprofloxacin, metronidazole) and/or immunomodulators (AZA, 6-MP, MTX).Please refer to Appendix 3 for details.
Note: Participants refractory, intolerant or dependent on corticosteroids will be
permitted to participate in the study.
6. Adhere to the following requirements for concomitant medication for the treatment of
Crohn's disease. The following medications are permitted if doses meeting the requirements listed below are stable or have been discontinued prior to baseline and
within the timeframes specified below:
• Oral corticosteroids at a prednisone-equivalent dose at or below 20 mg/day, or 6 mg/day of budesonide, or 5 mg/day beclomethasone dipropionate, and on stable dosing for at least 2 weeks or if recently discontinued, must have been stopped for
at least 2 weeks.
• Conventional immunomodulators (ie, AZA, 6-MP, or MTX) for at least 12 weeks and have been on a stable dose for at least 4 weeks or if recently discontinued, must
have been stopped for at least 4 weeks.
• If receiving antibiotics as a primary treatment of luminal Crohn's disease, all
antibiotics must be stopped prior to baseline.
7. If receiving enteral nutrition as a primary treatment for Crohn*s disease, must have been
receiving for at least 2 weeks or if recently discontinued, must have been stopped for at
least 2 weeks.
8. Screening laboratory test results within the following parameters, and if 1 or more of
the laboratory parameters is out of range, a single retest of laboratory values is permitted
during the approximate 6-week screening period:
• Hemoglobin >=8.0 g/dL.
• White blood cells (WBCs) >=3.5 x 103/µL.

• Neutrophils >=1.5 x 103/µL.
• Platelets >=100 x 103/µL.
• Serum creatinine <=1.5 mg/dL.
• Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations must be <=2 times the upper limit of normal range for the laboratory conducting the test.
• Direct (conjugated) bilirubin <1.0 mg/dL.
Must be otherwise healthy based on clinical laboratory tests performed at screening. If the results of the serum chemistry panel (including liver enzymes, hematology, or urinalysis) are outside the normal reference ranges, the participant may be included only if the investigator judges the abnormalities or deviations from normal to be not clinically significant or to be appropriate and reasonable for the population under study.
This determination must be recorded in the participant's source documents and initialed by the investigator.
9.1 Are considered eligible according to the following tuberculosis (TB) screening criteria:
• •Have no history of latent or active TB prior to screening. An exception is made for participants who have a history of latent TB and who have documentation of having completed appropriate treatment for latent TB within 5 years before the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous anti-tuberculosis treatment and provide appropriate documentation.
• Have no signs or symptoms suggestive of active TB upon medical history and/or physical examination.
• Have had no recent close contact with a person with active TB.
• Within 8 weeks prior to the first administration of study intervention, have a negative QuantiFERON-TB (or T-SPOT for sites in Japan) test result, or have a newly identified positive QuantiFERON-TB (or T-SPOT for sites in Japan) test in which active TB has been ruled out. Indeterminate or borderline results may have the test repeated one time during screening. Please refer to Appendix 6 for details.
Note: A negative tuberculin skin test result is additionally required if the QuantiFERON-TB test is not approved/registered in the country in which this protocol is being conducted. In Ukraine, while the QuantiFERON-TB test is not approved/registered, it is acceptable, and an additional tuberculin skin test is not required. The QuantiFERON-TB test and the tuberculin skin test are not required

at screening for participants with a history of latent TB, if active TB has been ruled
out, and if appropriate treatment has been completed as described above. Chest radiographs must be obtained, and a TB specialist should be consulted per local guidelines, in all cases when the QuantiFERON-TB test and/or the tuberculin skin test for TB is positive or repeatedly indeterminate. Please refer to Appendix 7 for
details.
• Have a chest radiograph (both posterior-anterior and lateral views, or per local/country regulations where applicable), taken <=12 weeks before the first administration of study intervention and read by a qualified radiologist or qualified
pulmonologist according to local clinical practice, with no evidence of current, active TB or old, inactive TB. A chest CT scan is also acceptable if obtained instead
of a chest radiograph outside of the protocol.
10. Male or female (according to their reproductive organs and functions assigned by
chromosomal complement).
11. A woman of childbearing potential must have a negative serum pregnancy test at
Screening and Week 0.
12. A woman must be (as defined in Section 10.21, Contraceptive and Barrier Guidance)
a. Not of childbearing potential
b. Of childbearing potential and
Practicing a highly effective method of contraception (failure rate of <1% per year
when used consistently and correctly) and agrees to remain on a highly effective method while receiving study intervention and until 12 weeks after last dose - the
end of relevant systemic exposure. The investigator should evaluate the potential
for contraceptive method failure (eg, non-compliance, recently initiated) in relationship to the first dose of study intervention. Examples of highly effective
methods of contraception are presented in Appendix 21. Contraceptive and Barrier Guidance. The method selected must meet local/regional regulations and guidelines for highly effective contraception.
13.1 A woman must agree not to donate eggs (ova, oocytes) for the purposes of assisted
reproduction during the study and for a period of 12 weeks after the last dose of the
study interventions.
14.1 A male participant must wear a condom when engaging in any activity that allo

Exclusion criteria

1. Has a very severe luminal disease activity (defined as CDAI >=350).
2. Has any of the following:
• history of or concurrent rectovaginal fistulas, rectal and/or anal stenosis (unless the participant undergoes surgical dilation prior to baseline), diverting stomas with anastomotic leakage, abscess or collections which are not properly drained.
• colonic mucosal dysplasia or pre-cancerous lesions that have not been removed, demyelinating disease, or systemic lupus erythematosus.
3. Has current complications of Crohn*s disease, such as symptomatic strictures or stenoses, short gut syndrome, or any other manifestation, that might be anticipated to require surgery, could preclude any fistula evaluation (both clinical and radiological) to assess response to therapy, or would possibly confound the ability to assess the effect of treatment with guselkumab.
4. Has a stool culture or other examination positive for an enteric pathogen, including Clostridioides difficile (formerly known as Clostridium difficile) toxin, in the previous 4 months, unless a repeat examination is negative and there are no signs of ongoing infection with that pathogen.
5. Has a history of, or ongoing, chronic or recurrent infectious disease, including but not limited to, chronic renal infection, chronic chest infection (eg, bronchiectasis), recurrent urinary tract infection (eg, recurrent pyelonephritis or chronic non-remitting cystitis), or open, draining, or infected skin wounds or ulcers.
6. Has a history of serious infection (eg, hepatitis, sepsis, pneumonia, or pyelonephritis), including any infection requiring hospitalization, during the 8 weeks before baseline.
7. Currently has a malignancy or has a history of malignancy within 5 years before screening (with the exception of a nonmelanoma skin cancer that has been adequately treated with no evidence of recurrence for at least 3 months [defined as a minimum of 12 weeks] before the first study intervention administration or cervical carcinoma in

situ that has been treated with no evidence of recurrence for at least 3 months before
the first study intervention administration).
8. Has a known history of lymphoproliferative disease, including lymphoma, or signs and
symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy, hepatomegaly, or splenomegaly, or monoclonal gammopathy of undetermined significance.
9. Has a history of severe, progressive, or uncontrolled renal, genitourinary, hepatic,
hematologic, endocrine, cardiac, vascular, pulmonary, rheumatologic, neurologic, psychiatric, or metabolic disturbances, or signs and symptoms thereof.
10. Has a transplanted organ (with exception of a corneal transplant >12 weeks before
screening).
11. Is unable or unwilling to undergo multiple venipunctures because of poor tolerability
or lack of adequate venous access.
12. Is unwilling to get a subcutaneous injection.
13. Has unstable suicidal ideation or suicidal behavior in the last 6 months that may be
defined as a Columbia-Suicide Severity Rating Scale (C-SSRS) rating at screening of:
Suicidal Ideation with Intention to Act (*Ideation level 4*), Suicidal Ideation with
Specific Plan and Intent (*Ideation level 5*), or suicidal behavior (actual suicide
attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors
for making a suicide attempt), and is considered to be at risk by the investigator based
on an evaluation by a mental health professional. In addition, participants with C-SSRS
ratings of Wish to be Dead (*Ideation level 1*), Non-Specific Active Suicidal Thoughts
(*Ideation level 2*), Active Suicidal Ideation with Any Methods (Not Plan) without
Intent to Act (*Ideation level 3*) or non-suicidal self-injurious behavior who are
determined to be at risk by the investigator may not be randomized.
14. Presence of ulcerative colitis, indeterminate colitis, ischemic colitis, fulminant colitis,
or toxic mega-colon.
15.1 Known allergies, hypersensitivity, or intolerance to guselkumab or its excipients (refer
to the Investigator Brochure [IB Guselkumab 2022]), ciprofloxacin
16. Contraindications to the use of guselkumab per local prescribing

information.
17.1 Has received any of the following prescribed medications or therapies within the
specified period:
• Intravenous corticosteroids received within 3 weeks of baseline
• Cyclosporine, tacrolimus, sirolimus, or mycophenolate mofetil received within 8
weeks of baseline
• 6-thioguanine received within 4 weeks of baseline
• Biologic agents:
• Anti-TNF therapy (eg, infliximab, etanercept, certolizumab pegol, adalimumab, golimumab) received within 4 weeks of baseline
• Vedolizumab received within 4 weeks of baseline
• Has previously received a biologic agent targeting IL-12/23 or IL-23, including but not limited to briakinumab, brazikumab, guselkumab, mirikizumab, tildrakizumab and risankizumab
Note: Participants with prior exposure to IL-12/23 or IL-23 agents are ineligible for entry into this protocol, with the exception of participants who have had exposure to ustekinumab at its approved labeled dosage AND have met the required washout criterion (16 weeks) AND have not demonstrated failure or intolerance to ustekinumab. Please refer to Appendix 5 for details.
• Other immunomodulatory biologic agents received within 4 weeks of baseline or within 5 half-lives of baseline, whichever is longer
• Any investigational intervention received within 4 weeks of baseline or within 5
half-lives of baseline, whichever is longer
• Non-autologous stem cell therapy (eg, Prochymal), autologous adipose-derived stem cells (eg, Darvadstrocel), natalizumab, efalizumab, or biologic agents that deplete B- or T-cells (eg, rituximab, alemtuzumab, or visilizumab) received within
6 months of baseline
• Treatment with apheresis (eg, Adacolumn apheresis) or parenteral nutrition for Crohn*s disease within 3 weeks of baseline
Has received, or is expected to receive, any live virus or bacterial vaccination within 4
weeks before the first administration of study intervention. For Bacille Calmette-
Guérin (BCG) vaccine, see Exclusion Criterion 18
18. Has had a BCG vaccination within 1 year of Screening.
19. Taken any disallowed therapies as noted in Section 6.8, Concomitant Therapy before
the planned first dose of study intervention.
20. Has received any investigational intervention received within 4 weeks of baseline or
within 5 half-lives of baseline, whichever is longer.
21.1 Is a woman who is pregnant, or breastfeeding, or planning to become pregnant while

enrolled in this study or within 12 weeks after the last administration of study intervention.
22.1 Plans to father a child while enrolled in this study or within 12 weeks after the last dose
of study intervention.
23.1 Any condition for which, in the opinion of the investigator, participation would not be
in the best interest of the participant (eg, compromise the well-being) or that could
prevent, limit, or confound the protocol-specified assessments. Vulnerable participants
under protective measures must be excluded from the study.
24.1 Have undergone previous surgery, other than drainage and/or seton placement and/or
fistula curettage for a draining fistula up to 6 weeks prior to baseline (Week 0). Had
major surgery, within 12 weeks before screening, or will not have fully recovered from
surgery, or has had any kind of bowel resection within 6 months, or any other intra-
abdominal or other major surgery within 12 weeks before baseline.
Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate
Infections or predisposition to infections
25. COVID-19 infection:
During the 6 weeks prior to baseline, has had any of the following: (a) confirmed severe
acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (test pos

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-11-2023
Enrollment:	11
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	guselkumab
Generic name:	Tremfya
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-06-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-10-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-06-2023
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-07-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-09-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-11-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-12-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-504740-33-00
EudraCT	EUCTR2021-000491-10-NL
CCMO	NL80774.028.22