A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Efficacy and Safety of Guselkumab Subcutaneous Induction Therapy in Participants With Moderately to Severely Active Crohn's Disease

Published: 17-02-2022
Last updated: 06-04-2024

Primary objective:- To evaluate the efficacy, including clinical remission and endoscopic response, of guselkumab SC inductionSecondary objectives:- To evaluate the efficacy of guselkumab SC across a range of outcome measures- To evaluate the safety…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON51325

Source
ToetsingOnline

Brief title
GRAVITI

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, 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: CNTO 1959, Crohn's Disease, Gravity

Outcome measures

Primary outcome

Primary endpoints:

- Clinical remission (CDAI score <150) at Week 12

- Endoscopic response (>=50% improvement from baseline in the SES-CD score) at Week 12

Secondary outcome

Secondary endpoints:

- Clinical remission at Week 24

- PRO-2 remission (an AP mean daily score <=1 and SF mean daily score <=3 and no worsening of AP or SF from baseline)at Week 12

- Clinical response (decrease from baseline in CDAI >=100 points or clinical remission) at Week 12

- Summary of AEs, such as SAEs and AEs leading to discontinuation of study intervention.

Study description

Background summary

Guselkumab is a fully human immunoglobulin G1 lambda monoclonal antibody that binds to the p19 protein subunit of human interleukin (IL)-23 with high specificity and affinity. By binding to the p19 subunit of IL-23, guselkumab blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23 mediated intracellular signaling, activation and cytokine production including IL-17A, IL-17F, and IL-22. A rapidly growing body of literature suggests that the IL-23 pathway contributes to the chronic inflammation underlying the pathophysiology of many immune-mediated diseases including psoriasis, psoriatic arthritis, ankylosing spondylitis, and inflammatory bowel disease (IBD).
Results from the GALAXI 1 study show that guselkumab IV induction demonstrated greater improvements compared to placebo across the key clinical efficacy and endoscopic outcome measures at Week 12 (Danese 2021; Sandborn 2020b). The safety profile of guselkumab in the GALAXI 1 study population is consistent with the safety profile of guselkumab established from clinical trials across investigational and approved indications. In summary, the collective nonclinical and clinical evidence for the critical role of IL-23 in the pathogenesis of Crohn*s disease, the benefit-risk profile of guselkumab established to date in psoriasis and other immune-mediated diseases, and the GALAXI 1 results provide a strong scientific and clinical rationale for pursuing development of guselkumab in patients with moderately to severely active Crohn*s disease and for the investigation of guselkumab in this study.

The proposed study is a part of guselkumab development program, and Crohn*s disease is one of the indications the study intervention is being investigated for. Guselkumab belongs to the group of biological medications which correspond to the advanced IBD therapy. Considering this, the study patients population will be represented by the subjects who have demonstrated inadequate response or failed to tolerate previous Crohn*s disease therapy (conventional and/or biological).
Currently, the GALAXI clinical program is evaluating guselkumab intravenous (IV) induction dosing followed by subcutaneous (SC) maintenance dosing in participants with moderately to severely active Crohn*s disease who have demonstrated an inadequate response or failure to tolerate previous conventional therapy or biologic therapy.
In the current study, the sponsor is interested in assessing SC administration of guselkumab for the induction phase of Crohn*s disease treatment. Subcutaneous delivery of biologic agents has become a valuable alternative to IV administration across many disease areas (Tetteh 2014; De Cock 2016; Gardulf 2007; Usmani 2021). In addition, SC administration has resulted in reduced drug delivery-related healthcare costs and resource utilization (Bittner 2018).

In short, SC administration has become an attractive alternative to more invasive and time-consuming IV infusions.

Study objective

Primary objective:
- To evaluate the efficacy, including clinical remission and endoscopic response, of guselkumab SC induction

Secondary objectives:
- To evaluate the efficacy of guselkumab SC across a range of outcome measures
- To evaluate the safety of guselkumab SC * Summary of AEs, such as SAEs and AEs

Study design

This is a randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of guselkumab subcutaneous (SC) induction dosing. The target population is adult participants with moderately to severely active Crohn*s disease (of at least 3 months duration) with colitis, ileitis, or ileocolitis previously confirmed by radiography, histology, and/or endoscopy. To be eligible for the study, participants must also have endoscopic evidence of active Crohn*s disease, and have demonstrated an inadequate response or failure to tolerate previous conventional therapy (oral corticosteroids or the immunomodulators azathioprine [AZA], 6-mercaptopurine [6-MP] or methotrexate [MTX]; CON-Failure) or biologic therapy (infliximab, adalimumab, certolizumab pegol, vedolizumab, or approved biosimilars for these agents; BIO-Failure).

Overall, the study will evaluate guselkumab SC treatment through 12 weeks of induction therapy and at least 12 weeks of maintenance therapy. At Week 24, all participants will enter the extension phase and receive the same treatment regimen that they were receiving at Week 24. The study will be unblinded after the last participant completes the Week 48 evaluations and the Week 48 database lock (DBL)is completed. Upon study unblinding, placebo participants who have not been rescued with guselkumab (see Intervention Groups and Duration section) will be discontinued from study intervention and have a final efficacy and safety (FES) follow-up visit. All other participants will continue on guselkumab treatment through Week 96.

In general, participants who are receiving oral 5-aminosalicylic acid compounds, oral corticosteroids, conventional immunomodulators (AZA, 6-MP, or MTX), antibiotics, and/or enteral nutrition for the treatment of Crohn*s disease at baseline should maintain a stable dose for a specified period before baseline and through Week 48, with the exception of oral corticosteroids. Starting at Week 12, all participants who were taking corticosteroids at Week 0

must begin tapering their corticosteroid dose. This tapering is mandatory, unless not medically feasible. Participants who discontinue study intervention early should return for a study intervention discontinuation (SID) visit. All randomized participants should complete the FES follow-up visit approximately 12 weeks after the last dose of study intervention.

Efficacy, safety, pharmacokinetics (PK), immunogenicity, and biomarkers will be assessed. A blood sample for harmacogenomic research will be collected only from participants who consent to this component of the protocol (where local regulations permit). Database locks are planned for Week 24, Week 48, and when the last participant completes the last scheduled assessment.

Intervention

At Week 0, eligible participants will be randomly assigned in a 1:1:1 ratio to one of the following SC
treatments:
* 106 participants to guselkumab 400 mg SC at Weeks 0, 4, and 8 followed by guselkumab 200 mg SC every 4 weeks (q4w) through Week 24
* 106 participants to guselkumab 400 mg SC at Weeks 0, 4, and 8 followed by guselkumab 100 mg SC every 8 weeks (q8w) through Week 24
* 106 participants to placebo SC q4w from Week 0 through Week 24

The randomization will be stratified by baseline Crohn*s Disease Activity Index (CDAI) score (<=300 or >300), baseline Simple Endoscopic Score for Crohn*s Disease (SES-CD) score (<=12 or >12), and BIO-Failure status (Yes or No) at baseline (Week 0).

During the extension phase, all participants will continue to receive the same treatment regimen that they were receiving at Week 24.

Upon study unblinding after Week 48 DBL, placebo participants who have not been rescued with guselkumab will be discontinued from study intervention and have an FES follow-up visit. All other participants will continue on guselkumab treatment through Week 96.

All participants in the placebo group who meet at least 1 of the rescue criteria at Weeks 12 and 16 will receive rescue treatment, ie, guselkumab 400 mg SC at Weeks 16, 20, and 24 followed by guselkumab 100 mg SC every 8 weeks (q8w). To maintain the blind, participants randomized to guselkumab who meet at least 1 of the rescue criteria will continue their assigned treatment regimen and receive blinded sham rescue matching placebo SC injection.

All participants in the placebo group who meet at least 1 of the following rescue criteria will receive rescue medication:
* CDAI score >220 and <70-point reduction from baseline CDAI at both Week 12 and Week 16 OR

* SES-CD score increase by at least 50% from baseline at Week 12

Upon meeting at least 1 of the rescue criteria, participants in the placebo group will receive guselkumab 400 mg SC at Weeks 16, 20, and 24 followed by guselkumab 100 mg SC q8w.

Study burden and risks

For this study, the subjects will come to the center approximately 28 times (a number of visits may also be made by telephone). The study load includes:

- Blood draw 5x
- Urine test for pregnancy (max 28 visits)
- Subcutaneous injections 24x
- Intravenous injection 5x
- Chest x-Ray at screening 1x
- EKG at screening 1x
- Video Ileocolonscopy with biopsies 5x
- Physical examination (max 28 visits)
- Various interviews and questionnaires
- Stool samples for screening and biomarkers max.
- Fistula assessment (max 28 visits)
- QuantiFERON-TB blood test at sceening 1x

The subject may experience physical or psychological discomfort from the above tests, procedures and questionnaires.

The subject may experience side effects from the study medication.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Man or woman (according to their reproductive organs and functions assigned by chromosomal complement) of >=18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place).
2. Have Crohn*s disease or fistulizing Crohn*s disease of at least 3 months duration (defined as a minimum of 12 weeks), with colitis, ileitis, or ileocolitis, confirmed at any time in the past by radiography, histology, and/or endoscopy.
3. Have clinically active Crohn*s disease, defined as a baseline CDAI score >=220 but <=450 and either:
a. Mean daily SF count >=4, based on the unweighted CDAI component of the number of liquid or very soft stools. OR
b. Mean daily AP score >=2, based on the unweighted CDAI component of AP CNTO 1959 (guselkumab)
4. Have endoscopic evidence of active ileocolonic Crohn*s disease as assessed by central endoscopy reading at the screening endoscopy (SoA [Section 1.3]) defined as a screening SES-CD score >=6 (or >=4 for participants with isolated ileal disease), based on the presence of ulceration in at least 1 of the 5 ileocolonic segments, resulting in the following specified ulceration component scores:
a. A minimum score of 1 for the component of *size of ulcers* AND
b. A minimum score of 1 for the component of *ulcerated surface*
5. A participant who has had extensive colitis for >=8 years, or disease limited to a segment of the colon for >=10 years, must:
a. Have had a full colonoscopy to assess for the presence of dysplasia within 1 year before the first dose of study intervention. OR
b. Has a full colonoscopy with biopsy surveillance for dysplasia as the baseline endoscopy during the screening period. Results from these surveillance biopsies must be negative for dysplasia (low-grade, high-grade, or *indefinite

dysplasia in reactive atypia*) prior to the first dose of study intervention.

Concomitant or Previous Medical Therapies Received
6. Prior or current medication for Crohn*s disease must include at least 1 of the following, and must fulfill additional criteria as described in Appendix 2 (Section 10.2) and Appendix 3 (Section 10.3)as applicable:
a. Current treatment with oral corticosteroids (including budesonide and beclomethasone dipropionate) and/or immunomodulators (AZA, 6-MP, MTX) OR
b. History of failure to respond to, or tolerate, at least 1 of the following therapies: oral corticosteroids (including budesonide and beclomethasone dipropionate) or immunomodulators (AZA, 6-MP, MTX) OR
c. History of corticosteroid dependence (ie, an inability to successfully taper corticosteroids without a return of the symptoms of Crohn*s disease) OR
d. Has previously demonstrated lack of initial response (ie, primary nonresponders), responded initially but then lost response with continued therapy (ie, secondary nonresponders), or were intolerant to 1 or more biologic agents at a dose that is, at minimum, a locally approved dose for the treatment of Crohn's disease (ie, infliximab, adalimumab, certolizumab pegol, vedolizumab, or approved biosimilars for these agents)
Note: Participants meeting criteria 6a-c may either be naïve to biologic therapy (ie, infliximab, adalimumab, certolizumab pegol, vedolizumab, or approved biosimilars for these agents) or may have been exposed to these biologic therapies and did not demonstrate an inadequate response or intolerance.
7. Adhere to all of the following requirements for concomitant medication for the treatment of Crohn*s disease. The following medications are permitted provided that doses meeting the requirements listed below are stable or have been discontinued prior to baseline within the timeframes specified below:
a. Oral 5-ASA compounds on stable doses for at least 2 weeks; or if recently discontinued, must have been stopped for at least 2 weeks.
b. Oral corticosteroids at a prednisone-equivalent dose at or below 40 mg/day, or 9 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.
c. 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.
d. If receiving antibiotics as a primary treatment of Crohn*s disease, doses must be stable for at least 3 weeks; or if recently discontinued, must have been stopped for at least 3 weeks.
e. 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.

Screening Laboratory Tests
8. Have screening laboratory test results within the following parameters, and if 1 or more of the laboratory parameters are out of range, a single retest of

laboratory values is permitted during the approximately 5-week screening period:
a. Hemoglobin >=8.0 g/dL
b. White blood cells (WBCs) >=3.0 x 10 exponent 3 /µL
c. Neutrophils >=1.5 x 10 exponent 3 /µL
d. Platelets >=100 x 10 exponent 3 /µL
e. Serum creatinine <=1.5 mg/dL
f. Alanine transaminase (ALT) (or aspartate transaminase [AST])<=2 x upper limit of normal (ULN)
g. Total bilirubin (TBili) <=1.5 x ULN (Isolated total bilirubin >1.5 x ULN is allowed for those participants with known Gilbert*s syndrome. Gilbert*s syndrome is suggested by direct bilirubin <30% [Palmer 2020].)

Tuberculosis
9. A potential participant is considered eligible if the participant meets all of the following TB screening criteria:
Note: Interferon gamma release assay (IGRA) testing includes either QuantiFERON-TB® or T-SPOT® .TB.
a. Have no history of active TB or show signs or symptoms suggestive of active TB upon medical history and/or physical examination at screening.
b. Have no history of latent TB prior to screening. An exception is made for participants who have a history of latent TB AND who satisfy one of the following criteria:
1) Currently receiving treatment for latent TB OR
2) Will initiate treatment for latent TB prior to the first administration of study intervention
Note: For participants with a history of treated latent TB there must be documentation of appropriate treatment prior to the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous TB treatment and provide appropriate documentation. IGRA testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB.
c. Have had no recent close contact with a person with active TB. If there has been contact, such participants are referred to a physician specializing in TB to determine if treatment is warranted or not. This evaluation must be adequately documented and, if treatment is recommended, the participant must be receiving appropriate treatment prior to the first administration of study intervention.
d. Have a negative IGRA test result within 2 months prior to the first administration of study intervention, or who:
- Have a history of adequately treated latent TB described above.
- Have a newly identified positive IGRA test result in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated prior to the first administration of study intervention.
- Have a false-positive IGRA test as determined by the following: * A suspected false-positive initial IGRA test must be repeated. If repeat testing is NOT positive, the participant must be referred to a physician specializing in TB to determine if the initial test can be considered a false-positive. This

evaluation must be adequately documented prior to the first administration of study intervention. If repeat testing is positive, however, it will be considered a true-positive and the participant is only eligible if active TB has been ruled out and appropriate treatment for latent TB has been initiated as described
above.
e. Have a chest radiograph (both posterior-anterior and lateral views, or per local/country regulations where applicable), or chest computed tomography (CT) within 3 months prior to the first administration of study intervention that shows no abnormalities suggestive of active or inactive TB.

Contraception
10. A woman of childbearing potential must have a negative serum pregnancy test result at screening.
11. Before randomization, a woman must be (as defined in Appendix 7 [Section 10.7])
a. Not of childbearing potential (refer to Section 10.7 for instances when a screening follicle stimulating hormone (FSH)test should be considered) OR
b. Of childbearing potential and
o If heterosexually active, 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. Note: The method selected must meet local/regional regulations/guidelines for highly effective contraception. Note: If a participant*s childbearing potential changes after start of the study (eg, a premenarchal woman experiences menarche) or the risk of pregnancy changes (eg, a woman who is not heterosexually active becomes active), a woman must begin using a highly effective method of contraception.
12. 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 administration of study intervention.
13. During the study and for at least 12 weeks after the last administration of study intervention, a male participant:
a. Who is sexually active with a female of childbearing potential must agree to use a barrier method of contraception (ie, condom with spermicidal foam/gel/film/cream/suppository or female condom/occlusive cap [diaphragm or cervical/vault caps] with spermicidal foal/gel/film/cream/suppository)
b. Who is sexually active with a pregnant female must use a condom
c. Must agree not to donate sperm for the purpose of reproduction

General
14. Each participant must sign an informed consent form (ICF) indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study.
15. Must sign a separate ICF if he or she agrees to provide an optional DNA sample for research (where local regulations permit). Refusal to give consent

for the optional DNA research sample does not exclude a participant from participation in the study.
16. Be willing and able to adhere to all specified requirements, including but not limited to completion of assessments, adherence to visit schedule, and compliance with the lifestyle restrictions.

Exclusion criteria

1. Has 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 the use of the CDAI to assess response to therapy, or would possibly confound the ability to assess the effect of treatment with guselkumab.
2. Currently has or is suspected to have an abscess. Recent cutaneous and perianal abscesses are not exclusionary if drained and adequately treated at least 3 weeks before baseline, or 8 weeks before baseline for intra-abdominal abscesses, provided that there is no anticipated need for any further surgery. Participants with active fistulas may be included if there is no anticipation of a need for surgery and no abscesses are currently identified.
3. Has had any kind of bowel resection within 24 weeks, or any other intra-abdominal or other major surgery within 12 weeks, before first dose of study intervention.
4. Has a draining (ie, functioning) stoma or ostomy.
5. Presence on screening endoscopy of adenomatous colonic polyps, if not removed before study entry, or history of adenomatous colonic polyps that were not removed.
6. Has a stool culture or other examination positive for an enteric pathogen, including Clostridioides difficile (formerly known as Clostridium difficile) toxin, within 4 months before the first dose of study intervention, unless a repeat examination is negative and there are no signs of ongoing infection with that pathogen.

Concomitant or Previous Medical Therapies Received
7. Has received any of the following prescribed medications or therapies within the specified period:
a. IV corticosteroids received within 3 weeks of baseline
b. Cyclosporine, tacrolimus, sirolimus, or mycophenolate mofetil received within 8 weeks of baseline
c. 6-thioguanine received within 4 weeks of baseline
d. Biologic agents:
1) Anti-TNFα therapy (eg, infliximab, etanercept, certolizumab pegol, adalimumab, golimumab) received within 8 weeks of baseline
2) Vedolizumab received within 12 weeks of baseline
3) Other immunomodulatory biologic agents, including approved and investigational biologic agents, received within 12 weeks of baseline or within

5 half-lives of baseline, whichever is longer
e. Any investigational intervention received within 4 weeks of baseline or within 5 half-lives of baseline, whichever is longer. (Refer to exclusion criterion 7.d.3 for investigational biologic agents).
f. Non-autologous stem cell therapy (eg, Prochymal), natalizumab, efalizumab, or biologic agents that deplete B- or T-cells (eg, rituximab, alemtuzumab, or visilizumab) received within 12 months of baseline.
g. Treatment with apheresis (eg, Adacolumn apheresis) or total parenteral nutrition for Crohn*s disease within 3 weeks of baseline.
8. Has previously received a biologic agent targeting IL-12/23 or IL-23, including but not limited to ustekinumab, briakinumab, brazikumab, guselkumab, mirikizumab, and risankizumab.

Infections or Predisposition to Infections:
9. Has a history of latent or active granulomatous infection, including histoplasmosis or coccidioidomycosis, before screening. Participants with radiographic evidence of possible prior histoplasmosis or coccidioidomycosis will be excluded.
10. Has a history of, or ongoing, chronic or recurrent infectious disease, including but not limited to, sinopulmonary infections, bronchiectasis, recurrent renal/urinary tract infections (eg, pyelonephritis, cystitis), an open, draining, or infected skin wound, or an ulcer.
11. Chest radiograph must be obtained within 12 weeks before the first dose of study intervention. Results that shows an abnormality suggestive of an undiagnosed pulmonary pathology including but not limited to a malignancy, a previously unrecognized pulmonary pathology, as well as active or latent infections from TB, histoplasmosis, or coccidiomycosis would be exclusionary. A chest CT scan obtained outside of the protocol instead of a chest radiograph is also acceptable. Refer to inclusion criteria 9 for information regarding eligibility with a history of latent TB.
12. History of human immunodeficiency virus (HIV) antibody positive, or tests positive for HIV at screening.
13. Is seropositive for antibodies to hepatitis C virus (HCV), unless they satisfy one of the following conditions:
a. Has a history of successful treatment, defined as being negative for HCV RNA at least 12 weeks after completing antiviral treatment, and has a negative HCV RNA test result at screening, OR
b. While seropositive has a negative HCV RNA test result at least 12 weeks prior to screening and a negative HCV RNA test result at screening.
14. Tests positive for hepatitis B virus (HBV) infection (Appendix 4[Section 10.4]).
15. Bacille Calmette-Guérin (BCG) vaccination within 12 months or any other live bacterial or live viral vaccination within 4 weeks prior to screening, or plans to receive such vaccines during the study.
16. Has or has had a nontuberculous mycobacterial infection or clinically significant opportunistic infection (eg, cytomegalovirus colitis, pneumocystosis, invasive aspergillosis).

17. Has had a clinically significant infection (ie, hepatitis, sepsis, pneumonia, or pyelonephritis), has been hospitalized for an infection, or has been treated with parenteral antibiotics for an infection within 8 weeks before the first dose of study intervention. Treated and resolved infections not considered clinically significant at the discretion of the investigator need not be exclusionary (ie, acute upper respiratory tract infection, uncomplicated urinary tract infection).
18. Has current signs or symptoms of a clinically significant infection. Ongoing infections not considered clinically significant at the discretion of the investigator need not be exclusionary (ie, acute upper respiratory tract infection, uncomplicated urinary tract infection).
19. Has evidence of a herpes zoster infection within 8 weeks before the first dose of study intervention.
20. During the 6 weeks prior to baseline, have had ANY of (a) confirmed severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (Coronavirus Disease 2019 [COVID-19]) infection (test positive), OR (b) suspected SARS-CoV-2 infection (clinical features without documented test results), OR (c) close contact with a person with known or suspected SARS-CoV-2 infection Exception: May be included with a documented negative result for a validated SARS-CoV-2 test
a. Obtained at least 2 weeks after conditions (a), (b), (c) above (timed from resolution of key clinical features ifpresent, eg, fever, cough, dyspnea) AND
b. With absence of ALL conditions (a), (b), (c) above during the period between the negative test result and the baseline study visit
Note on COVID-19-related exclusion:
* The field of COVID-19-related testing (for presence of, and immunity to, the SARS-CoV-2 virus) is rapidly evolving. Additional testing may be performed as part of screening and/or during the study if deemed necessary by the investigator and in accordance with current regulations/guidance from authorities/standards of care.
* Precaution: for those who may carry a higher risk for severe COVID-19 illness, follow guidance from local health authorities when weighing the potential benefits and risks of enrolling in the study, and during participation in the study.

Malignancy or Increased Potential for Malignancy:
21. 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 dose of study intervention or cervical carcinoma in situ that has been treated with no evidence of recurrence for at least 3 months before the first dose of study intervention).
22. Has a known history of lymphoproliferative disease, including lymphoma, a history of monoclonal gammopathy of undetermined significance; or signs and symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy or splenomegaly.

Coexisting Medical Conditions or Past Medical History

23. Has a history of severe, progressive, or uncontrolled renal, genitourinary, hematologic, endocrine, cardiac, vascular, pulmonary, rheumatologic, neurologic, psychiatric, or metabolic disturbances, or signs and symptoms thereof.
24. Has a transplanted organ (with exception of a corneal transplant >12 weeks before screening).
25. Poor tolerability of venipuncture or lacks adequate venous access for required blood sample collections during the study period.
26. History of drug or alcohol abuse according to Diagnostic and Statistical Manual of Disorders (5th edition) criteria within 1 year before screening.
27. 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.
28. Has known allergy, hypersensitivity, or intolerance to guselkumab or its excipients (refer to the guselkumab IB).
29. 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 dose of study intervention.
30. Is a man who plans to father a child while enrolled in this study or within 12 weeks after the last dose of study intervention.

General
31. Currently participating or intends to participate in any other study using an investigational agent or procedure during the conduct of this study.
32. Has 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.
33. Is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.

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:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	TREMFYA®
Generic name:	Guselkumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	17-02-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-04-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-05-2022
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-09-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-10-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-10-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-01-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-03-2023
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
EudraCT	EUCTR2020-006165-11-NL
ClinicalTrials.gov	NCT05197049
CCMO	NL79992.028.22