# A Phase 3, Multicenter, Randomized, Double-Blind, Placebo- and Active-Controlled, Treat-Through Study to Evaluate the Efficacy and Safety of Mirikizumab in Patients with Moderately to Severely Active Crohn's Disease

Published: 27-06-2019
Last updated: 17-01-2025

MAIN Trial:Primary:To evaluate whether the efficacy of mirikizumab is superior to placebo in participants with Crohn's disease as assessed by- clinical response by patient reported outcome (PRO) at Week 12 andendoscopic response at Week 52-...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Gastrointestinal inflammatory conditions |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON52841

**Source**
ToetsingOnline

**Brief title**
I6T-MC-AMAM (VIVID-1)

### Condition

- Gastrointestinal inflammatory conditions

**Synonym**
Inflammatory bowel disease

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Eli Lilly
**Source(s) of monetary or material Support:** Eli Lilly and Company

## Intervention

**Keyword:** Crohn's Disease, Mirikizumab

## Outcome measures

**Primary outcome**

Main study:

1. Percentage of Participants Achieving Clinical Response and Endoscopic

Response

Clinical response by Patient Reported Outcome (PRO) based on stool

frequency (SF) and abdominal pain (AP)

Endoscopic response based on Simple Endoscopic Score for Crohn's Disease

(SES-CD) total score

2. Percentage of Participants Achieving Clinical Response and Clinical Remission

Clinical response by PRO based on SF and AP

Clinical remission based on CDAI

Adolescent Addendum:

Co-Primary

• The coprimary endpoint at Week 52 of:

o The proportion of patients achieving endoscopic response defined as a >=50%

reduction from baseline in SES-CD total score AND

o The proportion of patients achieving clinical remission by Patient Reported Outcome (PRO) (defined as SF <=3 and not worse than baseline [as per Bristol Stool Scale Category 6 or 7]) and abdominal pain (AP) <=1 and not worse than baseline

**Secondary outcome**

Main study:

1. Proportion of participants achieving endoscopic response based on Simple Endoscopic Score for Crohn's Disease SES-CD) total score

2. Proportion of participants achieving clinical remission by CDAI

3. Proportion of participants achieving endoscopic response based on SES-CD total score

4. Proportion of participants achieving endoscopic remission based on SES-CD total score

5. Percentage of Participants achieving clinical remission based on CDAI

6. Change from baseline in Urgency NRS

7. Percentage of Participants Achieving Clinical Response and Clinical Remission based on PRO

8. Percentage of Participants Achieving Clinical Response by PRO and Endoscopic Remission by SES-CD

9. Percentage of Participants Who Are Corticosteroid-free AND in Clinical Response by PRO AND either in Clinical Remission by CDAI or Endoscopic Remission by SES-CD

10. Change from Baseline in C-Reactive Protein

11. Change from Baseline in Fecal Calprotectin

12. Percentage of Participants Achieving Clinical Response by PRO with Extraintestinal Manifestations (EIMs) of Crohn's Disease

13. Percentage of participants achieving clinical response by PRO with fistulae response

14. Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Mirikizumab

15. Change from Baseline in Health Related Quality of Life based on Inflammatory Bowel Disease Questionnaire (IBDQ) score

Adolescent Addendum:

Secondary

• Proportion of patients achieving endoscopic response at Week 12

• Proportion of patients achieving clinical remission by PRO at Week 12

• Proportion of patients achieving endoscopic remission SES-CD <=4 (defined as SES-CD Total Score <=4 and at least a 2-point reduction from baseline and no subscore >1) at Week 52

• Proportion of patients taking corticosteroids at baseline achieving clinical remission by PRO or endoscopic remission SES-CD <=4 who were corticosteroid-free from Week 40 to Week 52

• Proportion of patients achieving remission by PRO in at least 80% of the visits from Week 12 to Week 52 (at least 9 of 11 visits)

• Proportion of patients achieving endoscopic response at both Week 12 and Week 52

• Proportion of patients achieving endoscopic remission SES-CD <=4 at Week 12

• Proportion of patients achieving clinical remission by CDAI at Week 12

• Proportion of patients achieving clinical remission by CDAI at Week 52

• Proportion of patients achieving clinical remission by PCDAI at Week 12

• Proportion of patients achieving clinical remission by PCDAI at Week 52

• Proportion of patients achieving endoscopic remission SES-CD <=4 at both Week 12 and Week 52

• Mean change from baseline at Week 12 and at Week 52:

o Urgency NRS

o IMPACT III score

• Change from baseline in the following biomarkers:

o C-reactive protein

o Fecal calprotectin

• Proportion of patients who had Crohn*s related emergency room visits

• Proportion of patients who had Crohn*s related hospitalizations

• Proportion of patients who had Crohn*s related surgeries

• Clearance and volume of distribution of mirikizumab

• Relationship between mirikizumab exposure and efficacy

• Observed height velocity by gender will be calculated at baseline, Week 12, Week 24, and Week 52

• Change from baseline in weight (kg) at all study visits by gender and age group

• Hormone levels will be evaluated

• Safety and tolerability data evaluation including but not limited to adverse

events, infections, injection-site reactions, clinical chemistry, haematology,

and immunogenicity

• Tolerability and acceptability of SC injection volumes of 2 ml + 1 ml

• (adverse events, including injection site reactions and pain, and treatment

discontinuation) assessed at regular intervals throughout the study

• Secondary analysis of the coprimary endpoint and all secondary endpoints in

the addendum

The other secondary and tertiary endpoints are described in section 4 of the

protocol.

# Study description

**Background summary**

AMAM Main Trial:
Mirikizumab (LY3074828) is a humanized immunoglobulin G4 (IgG4) monoclonal antibody that binds to the p19 subunit of interleukin-23 (IL-23), a cytokine that has been implicated in mucosal inflammation. Study I6T-MC-AMAM (AMAM) is a Phase 3 clinical trial designed to evaluate the safety and efficacy of mirikizumab in achieving endoscopic and clinical outcomes up to Week 52 in patients with moderately to severely active Crohn*s disease (CD). Patients who have an inadequate response to, loss of response to, or are intolerant to corticosteroid or immunomodulator therapy for CD (termed *conventional-failed*), and those who have an inadequate response to, loss of response to, or are intolerant to biologic therapy for CD (termed *biologic-failed*) will be included in the study.
AMAM Adolescent Addendum:
Crohn*s disease is similar in adult and pediatric/adolescent patients in terms of overall disease pathology and progression and potential treatment targets (Jakobson et. al. 2011). In addition, pediatric patients with CD are at increased risk of growth failure, retarded puberty, and reduced peak bone mass due to factors such as undernourishment, corticosteroid dependency, and pro-inflammatory cytokines (Gasparetto et al. 2014). According to both the Food and Drug Administration (FDA) (FDA Guidelines 2019) and European Medicines

Agency (EMA) (EMA Guidelines 2019), these marginal differences in disease pathology between pediatric and adult CD should not prohibit the inclusion of adolescents with CD into trials with adults.

**Study objective**

MAIN Trial:

Primary:
To evaluate whether the efficacy of mirikizumab is superior to placebo in participants with Crohn's disease as assessed by
- clinical response by patient reported outcome (PRO) at Week 12 and endoscopic response at Week 52
- clinical response by patient reported outcome (PRO) at Week 12 and clinical remission by Crohn's Disease Activity Index (CDAI) at Week 52

Major Secondary:
- To evaluate whether the efficacy of mirikizumab is superior to placebo as assessed by endoscopic response, endoscopic remission, clinical remission by CDAI, and Urgency NRS
- To evaluate the efficacy of mirikizumab in comparison to ustekinumab as assessed by endoscopic response, endoscopic remission, clinical remission by CDAI
- To evaluate the efficacy of mirikizumab in comparison to placebo in health outcomes and quality of life measures, symptomatic endpoints, inflammatory biomarkers
- To evaluate the pharmacokinetic and pharmacokinetic/pharmacodynamic relationships of mirikizumab

Adolescent Addendum:
Co-Primary
• To evaluate whether treatment with mirikizumab is superior to adult placebo as assessed by endoscopic response at Week 52 and clinical remission by PRO at Week 52
Secondary
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in endoscopic response at Week 12
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in clinical remission by PRO at Week 12
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in endoscopic remission at Week 52
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in corticosteroid-free clinical remission by PRO or endoscopic remission at Week 52
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in the stability of clinical remission by PRO through Week 52

• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in the durability of endoscopic response at Week 52
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in endoscopic remission at Week 12
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in clinical remission by CDAI
• To summarize the efficacy of treatment with mirikizumab in clinical remission by PCDAI
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in the durability of endoscopic remission through Week 52
• To evaluate the effect of mirikizumab compared to adult placebo on changes in health outcomes and quality of life measures
• To evaluate the effect of mirikizumab compared to adult placebo on changes in inflammatory biomarkers during the study
• To evaluate the effect of mirikizumab in reducing the proportion of ER visits for CD, hospitalizations for CD, and to undergo surgery for CD compared to adult placebo over the course of the study
• To evaluate the pharmacokinetic and pharmacokinetic/pharmacodynamic relationships of mirikizumab
• Mirikizumab treatment effect on height velocity at Weeks 12, 24, and 52
• To evaluate the effect of treatment with mirikizumab on weight gain throughout the trial
• To evaluate the effect of treatment with mirikizumab on pubertal development throughout the trial
• Evaluate the safety and tolerability of mirikizumab treatment
• Tolerability and acceptability of SC injection volumes of 2 ml + 1 ml
• Assess consistency of response in mirikizumab-treated adolescents compared with mirikizumab-treated adults
Tertiary/Exploratory
• To evaluate the effect of mirikizumab treatment on changes in health outcomes and quality of life measures
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in clinical response by PRO at Week 4, Week 12, or Week 52
• To determine the effect of treatment of mirikizumab on extraintestinal manifestations (EIMs) of CD compared to adult placebo at Week 52
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in endoscopic response and clinical response by PRO
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in endoscopic remission SES-CD Total Score 0 - 2
• To evaluate the efficacy of treatment with mirikizumab compared to adult placebo in (endoscopic remission and clinical remission by PRO) at Week 52
• To evaluate selected objectives in the conventional-failed and biologic-failed subgroups of patients compared to adult placebo
• To determine the effect of treatment of mirikizumab on closure of draining fistulae in patients with draining fistulae at baseline compared to adult placebo
• To evaluate histologic response (mucosal healing) between patients receiving

mirikizumab compared to adult patients receiving placebo at Week 52

The other secondary and tertiary goals are described in section 4 of the protocol.

**Study design**

Main study:
Study AMAM is a Phase 3, multicenter, randomized, double-blind, double-dummy, parallel group, placebo and active controlled, treat-through study to evaluate the safety and efficacy of mirikizumab compared to placebo and ustekinumab. The study population includes participants with moderately to severely active CD who have an inadequate response to, loss of response to, or intolerance to conventional or biologic therapy for CD.

This is a parallel, double-blinded treatment study with three groups in Period 1 and four groups in Period 2.

Adolescent Addendum:
This open-label addendum to the AMAM adult study will assess efficacy and safety of mirikizumab in the induction and maintenance of remission in adolescents (15 to <18 years of age) with moderately to severely active Crohn*s Disease. See Schema in Section 1.2 of the protocol.
Addendum participants with moderate-to-severe CD will be unblinded to treatment for the full duration of the study, though the study material assigned and dispensed is blinded (Section 6.3). During the induction period, participants will receive 900 mg mirikizumab by IV infusion doses at Weeks 0, 4, and 8. In the maintenance period, participants will receive 300 mg mirikizumab by SC injection every 4 weeks until Week 48.
Adult double-blind and double dummy placebo-treated participants will be used as the comparator for adolescent mirikizumab treated patients, noting:
• When Period 1 induction dosing concludes (Week 12), placebo responders continue receiving placebo, and nonresponders (NRs) at Week 12 will receive mirikizumab as described in the adult protocol.
The total duration of the combined treatment periods is up to 52 weeks.
The maximum total duration of study participation for each participant, including screening and the post-treatment follow-up period, is 73 weeks.

**Intervention**

Participants will be randomized in a 6:3:2 ratio to receive, respectively:
• A high dose Mirikizumab intravenously every 4 weeks for 3 doses, then a lower dose subcutaneously every 4 weeks
• A high dose Ustekinumab intravenously for one dose, then a lower dose subcutaneously every 8 weeks
• Placebo

o When Period 1 concludes (Week 12), responders continue receiving placebo, and
o Nonresponders (NR) to placebo at Week 12 will receive mirikizumab as described above.

To maintain blinding, participants receive placebo in a double-dummy manner.

The maximum total duration of study participation for each participant is 72 weeks, across the following study periods:

• Screening: up to 4 weeks
• Intervention Period 1: 12 weeks
• Intervention Period 2: 40 weeks
• Post-Treatment Follow Up: 12 to 16 weeks

**Study burden and risks**

Risks:
Clinical Study Exposure Safety information from 28 clinical studies in 4673 study participants who have taken the investigational product has been reviewed. This included 851 healthy adult participants, 2170 adult participants with psoriasis, 1442 adult participants with ulcerative colitis, 186 are adult participants with Crohn*s disease, and 24 are children under 18 years of age with ulcerative colitis or Crohn*s disease.

Some study participants have had the following side effects when taking the investigational product. Common side effects (1 or more out of 100 patients) when taking the investigational product were: Pain, redness, or other symptoms at injection site, Upper respiratory infection, Headache, and Rash. Uncommon side effects (1 or more patients out of 1000) when taking the investigational product were: Strong reaction that occurs at the start or during infusion into a vein, and increases in blood tests that indicate problems with liver. Three study participants died after having serious side effects. The study doctor considered these side effects to be related to the investigational product: Heart attack, cancer of the colon that had spread to other parts of the body, and cancer of the cells in the lymph system.

Eleven study participants had life-threatening, serious side effects considered related to the investigational product. Infections of the kidney, lungs, and lining of the heart; Heart attack; Decreased blood flow to the heart; Cancer of the stomach lining; Blood clot in the brain; Severe allergic reaction, Increases in blood tests that indicate problems with the liver; Serious infection at a body location that was not identified when receiving blinded study drug

The investigational product has been given to 24 study participants who were children under 18 years of age with ulcerative colitis or Crohn*s disease. Side

effects reported in 2 or more participants who received the investigational product in these ongoing studies include: Fever (n = 7), Headache (n = 6), Pain at injection site (n = 5), Rash (n = 3), Vomiting (n = 3), Constipation (n = 2), and Tiredness (n = 2).

The subjects undergo a number of study procedures such as blood collections, TB test, hepatitis tests, ECG tests, X-ray scans, endoscopy and biopsy.
These procedures may also be accompanied by certain risks. The procedures may also have other unknown risks.
A full list of the risks are described in the Informed consent form.

Burden:
A total of 64 to 72 weeks of participation, with 17 visits. The treatment period is around 1 year, where subjects receive intravenous infusion of the medication Intravenous infusions take at least 90 minutes.
Patients may experience a return or worsening of their symptoms at any time during this study.
Patients are also requested to make daily entries into their electronic diary device
A full list of the burden of the study procedures is described in the protocol in the informed consent form

## Contacts

**Public**
Eli Lilly

Island House, Eastgate Business Park, Little Island na
Cork Co.
IE
**Scientific**
Eli Lilly

Island House, Eastgate Business Park, Little Island na
Cork Co.
IE

## Trial sites

### Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (16-17 years)
Adults (18-64 years)

## Inclusion criteria

1. (AMAM Main Trial): have given written informed consent approved by the Ethical Review Board (ERB) governing the site.
1. (AMAM Adolescent Addendum): the investigator, or a person designated by the investigator, will obtain written informed consent approved by the Ethical Review Board (ERB) from each study participant or the participant's parent/legal guardian and the subject*s assent, when applicable, before any study-specific activity is performed. The investigator will retain the original copy of each
participant's signed consent/assent document.
2. (AMAM Main Trial): are male or female patients >=18 and <=80 years of age at the time of initial screening.
2. (AMAM Adolescent Addendum):are male or female patients 15 to <18 years of age weighing >40 kgs with moderate to severely active CD as defined in points 5 and 6 below at the time of initial
screening/consent.
[2a] male patients: no male contraception required except in compliance with specific local
government study requirements,
[2b] female patients: women of childbearing potential:
A. must test negative for pregnancy prior to initiation of treatment as indicated by
a negative serum pregnancy test at the screening visit followed by a negative urine pregnancy test within 24 hours prior to exposure.
AND
B. must agree to either remain abstinent, if complete abstinence is their preferred
and usual lifestyle, or remain in same-sex relationships, if part of their preferred and usual lifestyle, without sexual relationships with males. Periodic abstinence (for example, calendar, ovulation, symptothermal, or post-ovulation methods), declaration of abstinence just for the duration of a trial, and withdrawal are not acceptable methods of contraception.
OR
must use 2 effective methods of contraception for the entirety of the study. Abstinence or contraception must continue following completion of study drug administration for 20 weeks.
i. Two effective methods of contraception (such as male or female condoms with spermicide, diaphragms with spermicide, or cervical sponges) will be

used. The participant may choose to use a double barrier method of contraception. Barrier protection methods without concomitant use of a spermicide are not a reliable or acceptable method. Thus, each barrier method must include use of a spermicide. It should be noted that the use of male and female condoms as a double barrier method is not considered acceptable because of the high failure rate when these methods are combined.
ii. Of note, 1 of the 2 methods of contraception may be a highly effective (less than 1% failure rate) method of contraception (such as combination oral contraceptives, implanted contraceptives, or intrauterine devices).
women not of childbearing potential may participate and include those who are:
A. infertile due to surgical sterilization (hysterectomy, bilateral oophorectomy, or
tubal ligation), congenital anomaly such as mullerian agenesis; or
B postmenopausal - defined as either:
i. a woman at least 40 years of age with an intact uterus, not on hormone therapy, who has had either
* cessation of menses for at least 1 year without an alternative medical cause AND
* at least 6 months of spontaneous amenorrhea with a folliclestimulating hormone (FSH) level >40 mIU/mL; or
ii. a woman 55 years or older not on hormone therapy, who has had at least 6 months of spontaneous amenorrhea; or
iii. a woman at least 55 years of age with a diagnosis of menopause prior to starting hormone replacement therapy.
[3] have venous access sufficient to allow blood sampling and IV administration as per the
protocol.
Disease-Specific Inclusion Criteria
[4] have had a diagnosis of CD or fistulizing CD established at least 3 months prior to
enrollment confirmed by clinical, endoscopic, and histological criteria.
Note: A histopathology report supporting the diagnosis of CD must be available in the
source documents prior to randomization, in order to satisfy this inclusion criterion. If a
histopathology report supporting the diagnosis of CD is not available in the source
documents prior to randomization, the investigator can obtain additional biopsies for this
purpose at the screening endoscopy (sent to the local histopathology laboratory).
[5] have moderately to severely active CD as defined by unweighted daily average SF >=4
(loose and watery stools defined as Bristol Stool Scale Category 6 or 7) AND/OR unweighted daily average AP >=2 at baseline (Visit 2).
[6] enrollment of a subset of participants with a SES-CD score >=3 and <7 (for

patients with isolated ileal disease SES-CD >=3 and <4) and presence of at least one large ulcer (in the ileum, colon, or both) that results in a minimum score of 2 for the component of *size of ulcers* and a minimum score of 1 for the component of *ulcerated surface*.
[7] Participants with a family history of colorectal cancer, personal history of increased
colorectal cancer risk, age >50 years, or other known risk factor must be up-to date on
colorectal cancer surveillance per local guidelines. If not, this documentation of negative
colorectal cancer surveillance may be performed according to local guidelines during
screening.
Prior Medication Failure Criteria
[8] Participants must have an inadequate response to, loss of response to, or intolerance to at
least 1 of the medications described in Inclusion Criterion [8a] OR [8b]. For the relevant
medication specified in these criteria, documentation of dose, frequency, route of
administration, and duration of the qualifying failure is required.
[8a] Conventional-failed patients: Patients who have an inadequate response to, loss
of response to, or are intolerant to at least one of the following medications:
o corticosteroids
* corticosteroid-refractory disease, defined as signs and/or symptoms of active CD despite oral prednisone (or equivalent) at doses of at least 30 mg/day for a minimum of 4 weeks.
* corticosteroid-dependent disease, defined as:
a. an inability to reduce corticosteroids below the equivalent of prednisone 10 mg/day or budesonide below 3 mg/day within 3 months of starting corticosteroids without a return of signs and/or symptoms of active CD;
or
b. a relapse within 3 months of completing a course of corticosteroids.
* history of intolerance of corticosteroids (which includes evidence of a side-effect sufficiently serious as to precluding continued treatment with corticosteroids including, but not limited to, Cushing*s syndrome, osteopenia/osteoporosis, hyperglycemia, or neuropsychiatric sideeffects, including insomnia, associated with corticosteroid treatment).
o immunomodulators:
* signs and/or symptoms of persistently active disease despite at least 3 months* treatment with one of the following:
* oral AZA (>=1.5 mg/kg/day) or 6-MP (>=0.75 mg/kg/day) or MTX 25 mg (intramuscular or SC weekly) or
* oral AZA or 6-MP within a therapeutic range as judged by thioguanine metabolite testing, or
* a combination of a thiopurine and allopurinol within a therapeutic range as

judged by thioguanine metabolite testing.
Discontinuation despite clinical benefit does not qualify as having failed or being
intolerant to CD conventional therapy.
[8b] Biologic-failed patients: Participants who have an inadequate response to, loss
of response to, or are intolerant to an approved biologic therapy for CD (such as
anti-TNF antibodies or anti-integrin antibodies). Investigators must be able to document an adequate history of induction and/or maintenance dose use.
Participants should fulfill 1 of the following criteria:
o Inadequate response: Signs and symptoms of persistently active disease despite induction treatment at the approved induction dosing, that was indicated in the product label at the time of use,
OR
o Loss of response: Recurrence of signs and symptoms of active disease following prior clinical benefit during treatment with approved maintenance dosing.
OR
o Intolerance: History of intolerance to inflixim

## Exclusion criteria

Participants will be excluded from study enrollment if they meet any of the following criteria
within the screening period, unless otherwise specified below.
For rescreening activities within the screening period, see Section 5.4.
Gastrointestinal Exclusion Criteria
[12] are participants who:
[12a] have a current diagnosis of UC, IBD-unclassified (formerly known as indeterminate
colitis).
[12b] currently have or are suspected to have an abscess. Recent cutaneous and perianal
abscesses are not exclusionary if drained, adequately treated and resolved at least 3 weeks
prior to baseline or 8 weeks prior to baseline for intra-abdominal abscesses, provided that
there is no anticipated need for any further surgery.
[13] have a stoma, ileoanal pouch or ostomy.
[14] have had a bowel resection within 6 months, or any kind of intra-abdominal surgery
within 3 months of baseline (Visit 2).
[15] have complications of CD such as symptomatic strictures or stenosis, short gut syndrome,

or any other manifestation that might be anticipated to require surgery within 6 months
after screening, could preclude the use of the SES-CD, CDAI, or PRO to assess response
to therapy, or would possibly confound the ability to assess the effect of treatment.
Adenoma, Dysplasia, and Gastrointestinal Cancer Exclusion Criteria
[16] have any history or current evidence of cancer of the gastrointestinal tract.
[17] have any current sporadic adenoma without dysplasia that has not been removed. Once
completely removed, the patient is eligible for study.
[18] have any evidence of colonic dysplasia.
Criteria for Discontinuing Prohibited Medications
[19] have received any of the following for treatment of CD within the time frames specified
below:
[19a] corticosteroid enemas, corticosteroid suppositories or a course of IV corticosteroids within 2 weeks prior to screening endoscopy.
[19b] 5-ASA enemas or 5-ASA suppositories within 2 weeks prior to screening endoscopy.
[19c] immunomodulatory medications, including oral cyclosporine, IV cyclosporine,
tacrolimus, mycophenolate mofetil, thalidomide or Janus kinase inhibitors within 4 weeks prior to the screening endoscopy.
* AZA, 6-MP, and MTX are allowed at stable doses (Appendix 10.7).
* Other immunomodulatory medications should be discussed with the sponsor prior to screening.
[19d] anti-TNF antibodies (for example, infliximab, adalimumab, or certolizumab pegol) within 4 weeks prior to screening endoscopy.
[19e] anti-integrin antibodies (for example, vedolizumab) within 4 weeks prior to
screening endoscopy.
[19f] agents that deplete B or T cells (for example, rituximab, alemtuzumab, or visilizumab) within 12 months of baseline (Visit 2). Patients remain excluded if there is evidence of persistent targeted lymphocyte depletion at the time of screening endoscopy.
[19g] any investigational nonbiologic therapy within 4 weeks prior to the screening
endoscopy or within 5 half-lives prior to the screening endoscopy, whichever is longer.
[19h] any investigational biologic therapy within 8 weeks prior to the screening endoscopy or within 5 half-lives prior to the screening endoscopy, whichever is longer.
[19i] leukocyte apheresis (leukapheresis, for example, Adacolumn) within 3 weeks prior to screening endoscopy.
[19j] interferon therapy within 8 weeks prior to screening endoscopy.

[19k] natalizumab within 12 months prior to screening endoscopy.
[20] have ever received anti-IL-23p19 antibodies (for example, risankizumab [BI-655066],
brazikumab [MEDI-2070], guselkumab [CNTO1959], or tildrakizumab [MK-3222]) for any indication, including investigational use.
[21] Subjects who discontinued an anti-IL 12/23p40 antibody (for example, ustekinumab) due
to primary nonresponse or secondary loss of response or intolerance OR who received
more than the IV induction dose and 1 SC dose are not eligible.
Note: Participants who have received up to the IV induction dose and one SC dose of
anti-IL 12/23p40 antibodies (for example, ustekinumab), may be enrolled. However,
these participants must have discontinued treatment for a nonclinical reason (for example,
change of insurance) and discontinued at least 8 weeks prior to screening endoscopy.
Enrollment of participants meeting this criterion will be limited to approximately 10% of
total enrollment.
[22] require systemic corticosteroids for non-CD conditions (except corticosteroids to treat
adrenal insufficiency).
Infectious Disease Exclusion Criteria
[23] are participants who
[23a] have evidence of active tuberculosis (TB), or
[23b] have a past history of active TB, without documented appropriate treatment by the
World Health Organization (WHO) and/or the Centers for Disease Control and Prevention (CDC), or
[23c] are diagnosed with latent tuberculosis infection (LTBI) at screening and/or have a
past history of LTBI and have not started a course of an appropriate TB prophylaxis regimen (Section 8.2.6).
Participants diagnosed with LTBI at screening and/or history of LTBI without appropriate treatment (aligned with WHO/CDC guidance in place at the time of treatment) may be allowed to rescreen and may be eligible for the study, provided they
fulfill all the criteria described in Section 8.2.6.
[24] have received a Bacillus Calmette-Guérin (BCG) vaccination within 12 months or
received live attenuated vaccine(s) within 3 months of screening or intend to receive such
during the study.
[25] have human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS).

[26] have acute or chronic hepatitis B infection; or test positive for hepatitis B virus (HBV) at
screening, which is defined as:
* positive for hepatitis B surface antigen (HBsAg+)
OR
* negative for hepatitis B surface antigen (HBsAg-) and positive for anti-hepatitis B
core antibody (anti-HBc+) in conjunction with detectable HBV DNA (see Section 8.2.8).
[27] have current hepatitis C infection; or test positive for hepatitis C virus (HCV) at
screening, defined as:
* positive for hepatitis C antibody and detectable HCV RNA (see Section 8.2.9).
Note: Participants with a previous HCV infection that has been successfully treated with
anti-viral therapy are not excluded (see Section 8.2.9).
[28] have tested positive for C. difficile toxin or for other intestinal pathogens within 30 days
of screening endoscopy or test positive at screening for C. difficile toxin or for other
intestinal pathogens. Participants with a confirmed diagnosis of cytomegalovirusassociated
colitis should have adequate treatment and resolution of symptoms at least 3 months prior to screening endoscopy (See Section 8.2.5).
[29] have serious, opportunistic, or chronic/recurring extraintestinal infections. Participants
may be eligible for entry into the study if they have been adequately treated and off
antibiotics for 30 days without recurrence of symptoms prior to screening. Such extraintestinal infections include but are not limited to the following:
[29a] infections requiring IV antibiotics.
[29b] infections requiring hospitalization.
[29c] infections that are considered *opportunistic* (see Appendix 10.5).
[29d] chronic, recurrent infections (for example, osteomyelitis, recurring cellulitis).
Participants with only recurrent, mild, and uncomplicated orolabial and/or genital
herpes may be discussed with the medical monitor to determine the relevance of this infection for entry into the study,
Participants with an opportunistic infection or chronic, recurrent infection (within
the last 60 days prior to Visit 2) should be discussed on a case-by-case basis with the
medical monitor.
[30] have a current or recent acute, active nonserious extraintestinal infection for which signs
and/or symptoms are present or treatment, if indicated, is not yet complete 2

weeks prior
to screening.
[31] have evidence of active/infectious herpes zoster infection <=8 weeks prior
to screening.
Herpes zoster infections remain active until all vesicles are dry and crusted

# 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: | Completed |
| Start date (anticipated): | 02-09-2020 |
| Enrollment: | 11 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Mirikizumab |
| Generic name: | Mirikizumab |
| Product type: | Medicine |
| Brand name: | Ustekinumab |
| Generic name: | Stelara |
| Registration: | Yes - NL intended use |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 27-06-2019 |
| Application type: | First submission |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 21-10-2019 |
| Application type: | First submission |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 20-01-2020 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 28-01-2020 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 22-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 24-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 24-08-2020 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 11-12-2020 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 18-01-2021 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 09-02-2021 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 24-03-2021 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 19-05-2021 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 30-04-2022 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 09-05-2022 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 10-06-2022 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 27-06-2022 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 10-09-2022 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 12-10-2022 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 31-10-2022 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 05-01-2023 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 12-01-2023 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 04-03-2023 |
| Application type: | Amendment |
| Review commission: | METC Brabant (Tilburg) |
| Approved WMO Date: | 16-05-2023 |
| 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 |
|---|---|
| Other | 03926130 |
| EudraCT | EUCTR2018-004614-18-NL |
| CCMO | NL69923.028.19 |

# Study results

Date completed: 31-01-2023

Results posted: 17-07-2024

Actual enrolment: 4

**First publication**
02-02-2024