A Phase 3, Multicentre, Open-Label, Long-Term Extension Study to Evaluate the Long-Term Efficacy and Safety of Mirikizumab in Patients with Crohn's Disease

Published: 18-05-2020
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This study has been transitioned to CTIS with ID 2022-502841-91-00 check the CTIS register for the current data. The main reason for this study is to help in answering the following research question: - Whether mirikizumab can help patients with...

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

Summary

ID

NL-OMON54068

Source
ToetsingOnline

Brief title
VIVID-2

Condition

- Gastrointestinal inflammatory conditions

Synonym
Bowel Inflammation, Crohn's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Eli Lilly (Sponsor)

Intervention

Keyword: Crohn's Disease, Mirikizumab

Outcome measures

Primary outcome

- Proportion of participants achieving clinical remission by CDAI (defined as

CDAI score <150) at Week 52 of AMAX

- Proportion of participants achieving endoscopic response (defined by >=50%

reduction from baseline in SES-CD Total Score) at Week 52 of AMAX

Secondary outcome

Key Secondary measures for subjects participating from study AMAM and that

achieved endpoints at Week 52:

1. Proportion of participants achieving endoscopic response at Week 156 of AMAX

2. Proportion of participants achieving endoscopic remission (defined as SES-CD

Total Score <=4 and at least a 2-point reduction from baseline and no sub-score

>1) in AMAX at:

a. Week 52

b. Week 156

3. Proportion of participants achieving clinical remission by PRO (defined as

SF <=3 and not worse than baseline [as per Bristol Stool Scale Category 6 or 7]

and AP <=1 and not worse than baseline) in AMAX at:

a. Week 52

b. Week 100

c. Week 156

4. Proportion of participants achieving clinical response by PRO (defined as at least a 30% decrease in stool frequency and/or abdominal pain, and no worse than baseline) in AMAX at:

a. Week 52

b. Week 100

c. Week 156

5. Proportion of participants achieving clinical remission by CDAI (CDAI score <150) in AMAX at:

a. Week 12

b. Week 52

c. Week 100

d. Week 156

6. Proportion of participants achieving endoscopic response in AMAX at:

a. Week 52

b. Week 156

7. Proportion of participants achieving clinical remission by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

8. Proportion of participants achieving clinical response by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

9. Proportion of participants who achieve clinical remission by PRO or endoscopic remission who are CS-free at Week 52 of AMAX

10. Proportion of participants who achieve clinical remission by PRO or endoscopic remission who are CS-free at Week 156 of AMAX

Key Secondary measures for subjects participating from study AMAM and that did not achieve endpoints at Week 52:

1. Proportion of participants achieving endoscopic response in AMAX at:

a. Week 52

b. Week 156

2. Proportion of participants achieving endoscopic remission in AMAX at:

a. Week 52

b. Week 156

3. Proportion of participants achieving clinical remission by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

4. Proportion of participants achieving clinical response by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

5. Proportion of participants achieving clinical remission by CDAI in AMAX at:

a. Week 52

b. Week 100

c. Week 156

6. To evaluate the following endpoints:

a. C-reactive protein at Week 12 of AMAX

b. Faecal calprotectin at Week 12 of AMAX

c. Proportion of participants with clinical response by PRO at Week 12 of AMAX

d. Proportion of participants with clinical remission by PRO at Week 12 of AMAX

7. Proportion of participants achieving endoscopic response in AMAX at:

a. Week 52

b. Week 156

8. Proportion of participants achieving clinical remission by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

9. Proportion of participants achieving clinical response by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

Key Secondary measures for subjects participating from study AMAM, irrespective of their prior treatment and endpoint achievement:

1. Proportion of participants achieving endoscopic response in AMAX at:

a. Week 52

b. Week 156

2. Proportion of participants achieving endoscopic remission in AMAX at:

a. Week 52

b. Week 156

3. Proportion of participants with clinical remission by PRO in AMAX at:

a. Week 52

b. Week 100

c. Week 156

4. Proportion of participants with clinical remission by CDAI in AMAX at:

a. Week 12

b. Week 52

c. Week 100

d. Week 156

5. Proportion of participants achieving CS-free clinical remission by PRO or endoscopic remission in AMAX at:

a. Week 52

b. Week 156

6. The following scores over time during AMAX:

a. Bowel Urgency NRS in AMAX at Week 12, Week 52, Week 100, and Week 156

b. WPAI-CD in AMAX at Week 12

c. EQ-5D-5L in AMAX at Week 12

d. FACIT-Fatigue in AMAX at Week 12, Week 52, Week 100, Week 156

e. IBDQ in AMAX at Week 12, Week 52, Week 100, Week 156

f. PGIC in AMAX at Week 12

g. PGRS in AMAX at Week 12, Week 52, Week 100, and Week 156

Study description

Background summary

A sizable proportion of the population with moderately-to-severely active Crohn's Disease (CD) is unresponsive to, fail to tolerate, or lose response to conventional therapies or approved biologic therapies

IL-23 which is a protein in the body plays a predominant role in inflammatory bowel disease (IBD). The relationship of this protein to IBD has been explored in several studies. The results of these studies indicate that IL-23 promotes intestinal inflammation. Data from some studies suggest that inhibition of IL-23 may provide efficacy in CD.

Mirikizumab binds the IL-23p19 subunit of human IL-23 and prevents binding of IL-23 to the IL-23 receptor, neutralizing the activity of human IL-23.

Several clinical studies of mirikizumab have been completed or are currently ongoing in patients with psoriasis, ulcerative colitis (UC), and CD. Mirikizumab has demonstrated efficacy in these studies. In the Phase 2 CD Study AMAG, treatment with mirikizumab has shown clinically relevant and consistent treatment effect in reducing or resolving endoscopic inflammation and patient-reported symptoms in patients with moderately-to-severely active CD. Evaluation of unblinded safety data in ongoing studies have shown a safety profile generally consistent with the IL-23 antibody class. Given the data from the Phase 2 study in CD and data from other clinical studies completed to date, potential benefits to participants who receive mirikizumab while participating in this study may be reasonably anticipated.

Study objective

This study has been transitioned to CTIS with ID 2022-502841-91-00 check the CTIS register for the current data.

The main reason for this study is to help in answering the following research question:
- Whether mirikizumab can help patients with Crohn*s disease when taken for a longer time.
- How safe mirikizumab is and whether you might have any side effects when you take it for a long time.

Study design

Study AMAX is a Phase 3, multicentre, long-term extension study evaluating the efficacy and safety of mirikizumab in participants with moderately-to-severely active Crohn's Disease (CD) who have participated in an originator adult mirikizumab CD study, inclusive of the Phase 3 Study AMAM and the Phase 2 Study AMAG.

Participants who are considered Responders (Response defined as >=50% reduction from baseline in SES-CD Total Score) in the originator Study AMAM and participants from Study AMAG will receive open-label mirikizumab subcutaneously (SC) for an extended period of time (up to 3 years) and then enter a 12- to 16-week post treatment follow-up period. Participants who are considered Non-responders in the originator Study AMAM will receive an induction treatment inclusive of 3 intravenous (IV) doses of mirikizumab and continue onto SC mirikizumab if clinical benefit is shown post-IV induction doses.

Participants who meet all of the inclusion criteria and none of the exclusion criteria of AMAX, and who, in the opinion of the investigator, would receive benefit from open-label treatment with mirikizumab are eligible for enrolment into Study AMAX. It is possible that some participants enrolling from Study AMAM may have received placebo only in the originating study. These participants will receive mirikizumab for the first time in Study AMAX.

Intervention

During the study, all participants will receive mirikizumab once every 4 weeks. All participants coming from Study AMAG will take mirikizumab as an injection under the skin. Participants coming from Study AMAM whose endoscopy results did not show the required improvement will receive their first 3 doses in this study as an intravenous (IV) injection. After the first 3 doses, participants from this group who show improvement will receive additional doses as injections under the skin. Other participants coming from Study AMAM whose endoscopy results showed the required improvement will take all doses of mirikizumab as injections under the skin.

Study burden and risks

Potential benefits to participants who receive mirikizumab while participating in Study AMAX may be reasonably anticipated, given the data obtained from the Phase 2 study in Crohn*s Disease (CD) and data from other clinical studies completed to date.

Immediate hypersensitivity reactions, including infusion-related hypersensitivity events consistent with anaphylaxis at the onset or during IV infusion of mirikizumab have been reported in ongoing studies. The protocol includes specific measures for reducing the incidence and for management of such events, including management of study drug infusion rate and observation

during and after infusion.

Detailed monitoring and management guidance will be provided to investigators, in the study protocol and Investigator*s Brochure (IB). This guidance is based on standard drug registration topics, safety findings from previous studies, potential risks, published literature, and co-morbidities and risk factors prevalent in the studied populations

In addition, an independent, external data monitoring committee (DMC) will review clinical trial data at pre-specified, regular intervals during the study. This independent assessment of clinical trial data will contribute to the overall ongoing evaluation and management of potential risks associated with mirikizumab administration.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Some of the important criteria for study participants to be eligible for inclusion in the study are (please refer section 5.1 of the protocol for more details):
1. They have given written informed consent
2. They have participated in the Phase 2 Study AMAG and have:
a. completed the last visit of participation in the AMAG study and remained on mirikizumab treatment in either the maintenance dosing period 3 or in the AMAG extension period, and
b. in the opinion of the investigator, would derive clinical benefit from continued treatment with mirikizumab.

It is preferred that participants receive the first dose of AMAX study drug within approximately 6-8 weeks of the last dosing visit in AMAG. A maximum of 18 weeks will be allowed between the last dose in AMAG and the first dose in AMAX to accommodate situations where due to circumstances outside the patient's control, a patient may not be able to complete all required assessments within the recommended shorter window.

3. They have participated in the Phase 3 Study AMAM and have:
a. completed Week 52 of the AMAM study, including the Week 52 endoscopy for evaluation of Responder/Non-responder status, and in the opinion of the investigator would derive clinical benefit from treatment with mirikizumab.

It is preferred that participants receive the first dose of AMAX study drug within approximately 6-8 weeks after the last dosing visit in AMAM. A maximum of 18 weeks will be allowed between the last dose in AMAM and the first dose in AMAX to accommodate situations where due to circumstances outside the patient's control, a patient may not be able to complete all required assessments within the recommended shorter window.

4. They are willing and able to complete the scheduled study assessments, including endoscopy, self-administer investigational product (or have caregiver administer investigational product), and complete patient electronic and paper diary.
5. They have clinically acceptable central laboratory test results at study entry which would not have resulted in permanent discontinuation of treatment in the originator study.
6. Contraception
a. Male Participants: No male contraception is required
b. Female Participants:
i. Women of childbearing potential: must test negative for pregnancy prior to initiation of treatment as indicated by a negative urine pregnancy test at Visit 1/Week 0 of this study
AND

ii. 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
iii. must use a combination of 2 effective methods of contraception or 1 highly effective method of contraception for the entirety of the study. Abstinence or contraception must continue following completion of study drug administration for 16 weeks.
iv. Women not of childbearing potential may participate and include those who are:
a) infertile due to surgical sterilization (total hysterectomy, bilateral salpingo-oophorectomy, bilateral salpingectomy, bilateral oophorectomy or tubal ligation), a congenital anomaly such as Müllerian agenesis, or
b) postmenopausal

Exclusion criteria

Some of the important criteria for study participants to be excluded from the study are (please refer section 5.2 of the protocol for more details):

3. They had a reported serious adverse event (SAE) in originator study or developed other condition prior to AMAX Week 0 that would disqualify them from treatment with mirikizumab according to originator study criteria.
4. Had permanently discontinued study drug in the originator study or had a temporary interruption of study drug in originator study such that, in the opinion of the investigator or Sponsor, restarting of mirikizumab would pose an unacceptable risk for the participant in Study AMAX.
5. Presence of significant uncontrolled neuropsychiatric disorder or judged at risk of suicide in the opinion of the investigator
6. Have a known hypersensitivity to any component of this investigational product or monoclonal antibodies or has experienced an acute systemic hypersensitivity event with previous study drug administration that precludes mirikizumab therapy.
7. Are pregnant, lactating, or planning to become pregnant while enrolled in the study or within 16 weeks after receiving the last dose of study drug.

9. Intend to receive a Bacillus Calmette Guerin (BCG) vaccination or a live attenuated vaccine during the study.
10. Have any history or current evidence of cancer of the gastrointestinal tract.
11. Have any current sporadic adenoma without dysplasia that has not been removed. Once completely removed, the patient is eligible for the study.

12. Have any evidence of colonic dysplasia.
13. Are currently enrolled in any other clinical study involving an investigational product or any other type of medical research judged not to be scientifically or medically compatible with this study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-10-2020
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	mirikizumab
Generic name:	mirikizumab

Ethics review

Approved WMO Date:	18-05-2020
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-05-2020

Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-01-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-01-2022
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:	31-10-2022

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-11-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-12-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-09-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-11-2023
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	CTIS2022-502841-91-00
EudraCT	EUCTR2019-002687-27-NL
ClinicalTrials.gov	NCT04232553
CCMO	NL72760.028.20