A Multicenter, Randomized, Double-Blind, Placebo Controlled 52-Week Maintenance and an Open-Label Extension Study of the Efficacy and Safety of Risankizumab in Subjects with Crohn's Disease

Published: 08-08-2017
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This study has been transitioned to CTIS with ID 2023-506399-28-00 check the CTIS register for the current data. Sub-study 1: The objective of sub-study 1 is to evaluate the efficacy and safety of risankizumab versus placebo as maintenance therapy...

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

Summary

ID

NL-OMON54770

Source
ToetsingOnline

Brief title
M16-000

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, form of Irritable Bowel Disease (IBD)

Research involving

Human

Sponsors and support

Primary sponsor: Site Management & Monitoring
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: - Crohn's Disease, - Maintenance and Open-Label Extension study, - Responders of Induction Treatment, - Risankizumab

Outcome measures

Primary outcome

Percentage of participants with clinical remission per daily stool frequency

(SF) and average daily abdominal pain (AP) score at Week 52.

Percentage of participants with endoscopic response at Week 52.

Secondary outcome

1. Proportion of participants with clinical remission per Crohn's Disease

Activity Index (CDAI) at Week 52

2. Proportion of subjects with clinical remission at Week 52 among the subjects

with clinical remission in Week 0

3. Proportion of subjects with ulcer-free endoscopy at Week 52

4. Proportion of subjects with endoscopic remission at Week 52

5. Mean change of IBDQ total score at Week 52 from baseline of induction

6. Mean change of FACIT fatigue at Week 52 from baseline of induction

7. Proportion of subjects who discontinued corticosteroid use for 90 days and

achieved clinical remission at Week 52 in subjects taking steroids at baseline

(of induction).

8. Proportion of subjects with CDAI clinical response at Week 52

9. Proportion of subjects with clinical remission and endoscopic response at

Week 52

10. Proportion of subjects with enhanced clinical response at Week 52

11. Proportion of subjects with deep remission at Week 52

12. Proportion of subjects with resolution of EIMs at Week 52 in subjects with

any EIMs at baseline of induction

13. Proportion of subjects with CD-related hospitalizations through Week 52

14. Proportion of subjects without draining fistulas at Week 52 in subjects

with draining fistulas at baseline of induction

15. Proportion of subjects with CD-related surgeries through Week 52

Study description

Background summary

The aim of medical treatment in CD has been focused on controlling inflammation and reducing symptoms. In addition to improving symptoms, an emerging goal of therapy is to heal the gut mucosa. Resolution of intestinal ulcers, also known as mucosal healing has been associated with positive clinical benefits, including higher rates of clinical remission, fewer hospitalizations, and fewer abdominal surgeries. However, improvement of the appearance of the intestinal mucosa may be more difficult to achieve than symptomatic improvement alone.

Conventional pharmaceutical therapies (e.g., corticosteroids, aminosalicylates, thiopurines, methotrexate) are limited, do not always completely abate the inflammatory process, and have significant adverse effects. The advent of anti-TNFα agents (e.g., adalimumab) and integrin inhibitors (e.g., vedolizumab) have been shown to achieve clinical remission in patients refractory to conventional therapies.

Despite the benefits of available biologic therapies, many patients do not respond to initial treatment (primary loss of response) or lose treatment over time (secondary loss of response). Regarding anti-TNF agents, approximately 40%

of patients will experience primary non-response and secondary non-response occurs in 38% of patients at 6 months and 50% of patients at 1 year.. Therefore new therapeutic options are required in order to continue to improve the outcome of patients with CD.

Study objective

This study has been transitioned to CTIS with ID 2023-506399-28-00 check the CTIS register for the current data.

Sub-study 1: The objective of sub-study 1 is to evaluate the efficacy and safety of risankizumab versus placebo as maintenance therapy in subjects with moderately to severely active Crohn's disease (CD) who responded to risankizumab induction treatment in Study M16-006 or Study M15-991 and had a Baseline (of induction) eligibility SES-CD of >= 6 (>= 4 for isolated ileal disease).

Sub-study 2: The objective of sub-study 2 is to evaluate the efficacy and safety of two different dosing regimens for risankizumab as maintenance therapy in subjects with moderately to severely active CD who responded to induction treatment in Study M16-006 or Study M15-991.

Sub-study 3: The objective of sub-study 3 is to evaluate long-term safety of risankizumab in subjects who completed Sub-study 1 or 2 or M15-989, or subjects who responded to induction treatment in Study M16-006 or Study M15-991 with no final endoscopy due to the coronavirus SARS-CoV-2 pandemic. OL CTE to ensure uninterrupted care in accordance with local regulations until risankizumab is commercially available for participants who completed Sub-study 3.

Study design

This is a phase 3, multicenter, randomized, double-blind, placebo controlled 52-week maintenance and open-label extension study to assess the efficacy and safety of risankizumab in subjects with moderately to severely active Crohn's Disease who responded to induction treatment in M16-006 or M15-991 or completion of M15-989.

Intervention

Subjects receive once every eight weeks SC risankizumab or SC placebo. They receive this medication until the end of the study or till premature discontinuation. In Sub-study 2, the first dose may be IV or SC Risankizumab or placebo followed by once every 8 weeks of SC Risankizumab.

Study burden and risks

There will be higher burden for subjects participating in this trial compared to their standard of care. Subject will be visiting the hospital more frequently. During these visits study procedures will be performed including blood sampling and filling in questionnaires. Subjects will also be tested for TB. Subjects will also complete a daily diary. Women of Childbearing Potential should practice a method of birth control, during the study through at least 140 days after the last dose of study drug and are tested for pregnancy.

Subjects will either receive risankizumab and/or placebo during the study. The most common side effects reported during previous studies of risankizumab were nausea, abdominal pain, joint pain and headache.

The hypothesis that risankizumab should be effective in targeting inflammation in patients with Crohn's Disease who are unable to tolerate or who have had insufficient response to treatment with some current available medication, indicates that there is an acceptable rationale to conduct this study. The risks and burden associated with participating in this study are acceptable in regards to the potential benefit study subjects could possibly have.

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

1. Entry and completion of Study M16-006, Study M15-991 or Study M15-989. Completion includes the final endoscopy of Study M16-006, Study M15-991, or Study 989. The final endoscopy for studies M16-006 and M15-991 may be missing during the coronavirus SARS-CoV-2 pandemic due to local regulations prohibiting endoscopy and subjects may be allowed to enroll in Substudy 3 should they meet clinical response.
2. Achieved clinical response, defined as >= 30% decrease in average daily SF and/or >= 30% decrease in average daily AP score, and both not worse than Baseline of the induction study, at the last visit of Study M16-006 or Study M15-991. This is not applicable for subjects enrolling
from Study M15 989.
3. If female, subject must meet the criteria as stated in protocol Contraception Recommendations.

Exclusion criteria

- Subject is considered by the Investigator, for any reason, to be an unsuitable candidate for the study. Subjects should not be enrolled in Study M16-000 with high grade colonic dysplasia or colon cancer identified during Study M15-991 or during Study M15-989 if the final endoscopy was performed prior to enter M16-000
- Subject who has a known hypersensitivity to risankizumab or the excipients of any of the study drugs or the ingredients of CHO, or had an AE during Studies M16-006 or M15-991 or M15-989 that in the Investigator's judgment makes the subject unsuitable for this study.
- Subject is not in compliance with prior and concomitant medication requirements throughout
Studies M16-006 or M15-991.

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):	04-04-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Placebo
Generic name:	Placebo
Product type:	Medicine
Brand name:	Risankizumab
Generic name:	Risankizumab

Ethics review

Approved WMO Date:	08-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	15-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	01-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date: 15-07-2020

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 23-07-2020

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 08-10-2020

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 13-10-2020

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 06-03-2021

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 06-04-2021

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 08-06-2021

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 12-07-2021

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 29-07-2022

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date:	12-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	31-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO

Date:	25-07-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO

Date:	25-08-2023
Application type:	Amendment
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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	CTIS2023-506399-28-00
EudraCT	EUCTR2016-003191-50-NL
ClinicalTrials.gov	NCT03105102
CCMO	NL61179.018.17