A Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study of the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Crohn's Disease

Published: 10-08-2017
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The objective is to evaluate the efficacy and safety of risankizumab versus placebo during induction therapy in subjects with moderately to severely active CD.

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

Summary

ID

NL-OMON50722

Source
ToetsingOnline

Brief title
M16-006

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, Failed Prior Biologics, Induction Study, Risankizumab

Outcome measures

Primary outcome

Proportion of participants with clinical remission and proportion of

participants with endoscopic response at Week 12.

Secondary outcome

1. Proportion of subjects with CDAI clinical remission at Week 12

2. Proportion of subjects with CDAI clinical response at Week 4

3. Proportion of subjects with clinical remission at Week 4

4. Proportion of subjects with CDAI clinical response at Week 12

5. Mean change from baseline of induction in FACIT fatigue at Week 12

6. Mean change from baseline of induction in IBDQ total score at Week 12

7. Proportion of subjects with enhanced clinical response and endoscopic

response at Week 12

8. Proportion of subjects with endoscopic remission at Week 12

9. Proportion of subjects with enhanced clinical response at Week 4

10. Proportion of subjects with ulcer-free endoscopy at Week 12

11. Enhanced clinical response at Week 12

12. Proportion of subjects with resolution of extra-intestinal manifestations

(EIMs) at Week 12, in subjects with any EIMs at Baseline

13. Proportion of subjects with CD-related hospitalization through Week 12

14. Proportion of subjects without draining fistulas at Week 12 in subjects

with draining fistulas at Baseline

Study description

Background summary

The aim of medical treatment in Crohn*s disease (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-tumor necrosis factor alpha (TNFα) agents (e.g., adalimumab) and integrin inhibitors (e.g., vedolizumab) have been shown to achieve clinical remission in patients who are 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-TNFα 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. Additionally, some patients are not candidates for available biologic therapies. Therefore new therapeutic options are required in order to continue to improve the outcome of patients with CD.

Study objective

The objective is to evaluate the efficacy and safety of risankizumab versus placebo during induction therapy in subjects with moderately to severely active CD.

Study design

This is a phase 3 multicenter, randomized, double-Blind, placebo-controlled

induction study to assess the efficacy and safety of risankizumab in subjects with moderately to severely active CD.

Intervention

Subjects receive risankizumab or placebo, via IV, during the 12 week induction period (weeks 0 to 12); subjects with inadequate response receive risankizumab, via IV or SC, during the 12 week induction period 2 (week 12 to 24).

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, physical examinations, and filling in questionnaires. Subject will also be tested for TB, significant heart conditions, pregnancy, Hepatitis C/Hepatitis B and Human immunodeficiency virus (HIV). Subjects will also complete a daily symptom diary. Women of childbearing potential should practice a highly effective method of birth control, during the study through at least 140 days after the last dose of study drug.

Subjects will either receive risankizumab 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 CD 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

Public
Selecteer

Wegalaan 9
Hoofddorp 2132JD
NL
Scientific
Selecteer

Wegalaan 9

Hoofddorp 2132JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Males or females >= 18 and <= 80 years of age, or minimum age of adult consent according to local regulations, at the Baseline Visit. Where locally permissible,
subjects 16 to < 18 years of age who meet the definition of Tanner stage 5 for development at the Baseline Visit
- Diagnosis of CD for at least 3 months prior to Baseline
- Crohn's disease activity index (CDAI) score 220-450 at Baseline
- Confirmed diagnosis of moderate to severe CD as assessed by stool frequency (SF), abdominal pain (AP) score, and Simple Endoscopic Score for Crohn's Disease (SES-CD)
- Demonstrated intolerance or inadequate response to conventional or biologic therapy for CD
- If female, subject must meet the contraception recommendations

Exclusion criteria

- Subject with a current diagnosis of ulcerative colitis or indeterminate colitis
- Subjects with unstable doses of concomitant Crohn's disease therapy
- Receipt of Crohn's disease approved biologic agents prior to Baseline (as detailed in protocol), or any investigational biologic or other agent or procedure within minimally 35 days prior to the Baseline

- Prior exposure to p19 inhibitors (e.g., risankizumab)
- Complications of Crohn's disease (strictures, short bowel, etc)

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):	04-09-2018
Enrollment:	5
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:	10-08-2017

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-11-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-11-2017
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:	27-09-2018
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:	15-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2020
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:	03-06-2020

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:	25-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2016-003123-32-NL
ClinicalTrials.gov	NCT03105128
CCMO	NL60410.018.17

Study results

Date completed:	20-10-2020
Results posted:	01-10-2021

First publication
22-09-2021

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File