A Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Conventional and/or Biologic Therapies

Published: 08-03-2018
Last updated: 25-03-2025

The objective of this study is to evaluate the efficacy and safety of upadacitinib compared to placebo as induction therapy in participants with moderately and severely active Crohn's disease (CD).

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

Summary

ID

NL-OMON55413

Source
ToetsingOnline

Brief title
M14-433

Condition

- Gastrointestinal inflammatory conditions

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

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie B.V.
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: Crohn's Disease, Induction Study, Upadacitinib

Outcome measures

Primary outcome

Proportion of subjects with clinical remission per PROs at Week 12

Proportion of subjects with endoscopic response at Week 12

Secondary outcome

1. Proportion of subjects with clinical remission per CDAI (CDAI < 150)

2. Proportion of subjects with clinical remission at Week 4

3. Proportion of subjects with endoscopic remission at Week 12

4. Proportion of subjects who discontinue corticosteroid use for CD and

achieve clinical remission at Week 12, in subjects taking corticosteroids for

CD at Baseline

5. Change from Baseline in Functional Assessment of Chronic Illness

Therapy-Fatigue at Week 12

6. Change from Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) at

Week 12

7. Proportion of subjects achieving CR-100 at Week 2

8. Proportion of subjects achieving CR-100 at Week 12

9. Proportion of subjects with hospitalizations due to CD during the 12 week

double-blind induction period

10. Proportion of subjects with resolution of extra-intestinal manifestation

(EIM) at Week 12, in subjects with EIM at Baseline.

Study description

Background summary

Crohn's disease (CD) encompasses a spectrum of clinical and pathological processes manifested by focal asymmetric, transmural, and occasionally granulomatous inflammation that can affect any segment of the gastrointestinal tract. Crohn's disease has been characterized by significant morbidity including abdominal pain, diarrhea, weight lost/malnutrition, a progressive nature that leads to complications such as fistulas, strictures and abscesses. Given that no known medical or surgical cure currently exists for CD, the therapeutic strategy is to reduce symptoms, improve quality of life, reduce endoscopic evidence of inflammation, and minimize short and long-term toxicity and complications. Currently, patients with moderate to severe disease who have failed aminosalicylates or topical treatments are usually treated with conventional pharmacologic interventions, which include corticosteroids and immunosuppressive agents. Patients who do not respond to conventional therapies may be treated with biologics, such as antiTNF α therapies. However, approximately 40% of patients do not respond to their first biologic therapy (primary non-responders). Among patients who initially respond and continue to receive maintenance treatment for longer durations, approximately 38% become non-responders after 6 months and approximately 50% become non-responders at 1 year (secondary non-responders). The available treatment options may also be associated with some adverse events (AEs) that may limit the use or require close monitoring. Therefore, there remains a medical need for additional therapeutic options in CD for patients with inadequate response to or intolerance to conventional therapies and anti-TNF α agents.

Study objective

The objective of this study is to evaluate the efficacy and safety of upadacitinib compared to placebo as induction therapy in participants with moderately and severely active Crohn's disease (CD).

Study design

This is a phase 3, multicenter, randomized, double-blind, placebo-controlled induction study.

Intervention

All subjects receive upadacitinib or placebo once a day in the form of tablets (oral) until the end of the study or till premature discontinuation.

Study burden and risks

There will be higher burden for subjects participating in this trial compared to their standard of care. Subjects will be visiting the hospital more frequently. During these visits study procedures will be performed including blood sampling and completion of questionnaires. Subjects will be tested for TB, Hepatitis C/Hepatitis B and Human immunodeficiency virus (HIV) and subjects will also complete a daily diary. Women of Childbearing Potential should practice a method of birth control, during the study through at least 30 days after the last dose of study drug and are tested for pregnancy. Subjects will receive upadacitinib and/or placebo during the study. The most common side effects reported during studies of upadacitinib were headache, upper chest infection, common cold, diarrhea, and cough. The proposal to initiate a Phase 3 study in subjects with CD is based on the following supportive findings:
1) demonstrated clinical and endoscopic improvements in the induction treatment in a Phase 2 dose-ranging study; and
2) safety results were consistent with those known to be associated with JAK inhibition.
The current Phase 3 Study M14-433 will further evaluate the benefit to risk profile of upadacitinib in subjects with CD who have inadequately responded are intolerant to conventional therapies. 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)

Inclusion criteria

- Confirmed diagnosis of CD for at least 3 months prior to Baseline. Appropriate documentation of biopsy results consistent with the diagnosis of CD, in the assessment of the investigator, must be available.
- Evidence of mucosal inflammation based on the Simplified Endoscopic Score for Crohn's disease (SES-CD) on an endoscopy confirmed by a central reader.
- Confirmed diagnosis of moderate to severe CD as assessed by stool frequency (SF), abdominal pain (AP) score.
- Demonstrated an inadequate response or intolerance to one or more conventional and/or biologic therapies.
Note: Participants who have received prior biologic for up to 1 year but have not failed may be enrolled; however, participants must have discontinued the biologic for reasons other than inadequate response or intolerance (e.g., change of insurance, well controlled disease),
- If female, subject must meet the contraception recommendations.

Exclusion criteria

- Subject with a current diagnosis of ulcerative colitis or indeterminate colitis.
- Subject not on stable doses of CD related antibiotics, oral aminosalicylates, corticosteroids or methotrexate (MTX).

- Subject with the following known complications of CD: abscess (abdominal or peri-anal), > 2 entire missing segments of the following 5 segments: terminal

ileum, right colon, transverse colon, sigmoid and left colon, and rectum,symptomatic bowel strictures, fulminant colitis, toxic megacolon, or any other manifestation that might require surgery while enrolled in the study.
- Subject with ostomy or ileoanal pouch
- Subject diagnosed with conditions that could interfere with drug absorption including but not limited to short gut or short bowel syndrome

- Subject with surgical bowel resection within the past 3 months prior to baseline, or a history of >3 bowel resections.
- Subject laboratory and other analyses show abnormal results.

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):	13-05-2019
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Placebo
Generic name:	-
Product type:	Medicine
Brand name:	Upadacitinib

Generic name:	-

Ethics review

Approved WMO Date:	08-03-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	10-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2019
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:	16-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	13-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	09-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-10-2021
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	EUCTR2017-001240-35-NL
ClinicalTrials.gov	NCT03345849
CCMO	NL62827.018.18

Study results

Date completed:	23-08-2021
Results posted:	14-02-2023

First publication
23-11-2022

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

Internal documents
File