A Multicenter, Randomized, Double-Blind, Placebo- Controlled Maintenance and Long-Term Extension Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Crohn's Disease who Completed the Studies M14-431 or M14-433

Published: 08-03-2018
Last updated: 21-09-2024

This study has been transitioned to CTIS with ID 2023-504951-29-00 check the CTIS register for the current data. The objective of Substudy 1 (randomized, double-blind, placebo-controlled maintenance) is to evaluate the efficacy and safety of two...

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

Summary

ID

NL-OMON54751

Source
ToetsingOnline

Brief title
M14-430

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, Maintenance Study, Upadacitinib

Outcome measures

Primary outcome

Sub-study 1:

Proportion of subjects with clinical remission per PRO at Week 52, and

Proportion of subjects with endoscopic response at Week 52

Sub-study2:

Incidence of AEs over time

Secondary outcome

Sub-study 1:

1. Proportion of subjects with clinical remission per CDAI at Week 52

2. Proportion of subjects with endoscopic remission at Week 52

3. Change from Baseline in IBDQ at Week 52

4. Proportion of subjects achieving CR-100 at Week 52

5. Proportion of subjects without corticosteroid use for CD at least 90 days

prior to Week 52 and achieved clinical remission per PROs at Week 52 (among all

subjects)

6. Proportion of subjects who discontinued corticosteroid use for CD at least

90 days prior to Week 52 and achieved clinical remission per PROs at Week 52 in subjects taking corticosteroids for CD at Baseline of induction

7. Proportion of subjects with clinical remission per PROs at Week 0 and Week 52 (as measured by the proportion of subjects with clinical remission at Week 52 among those with clinical remission at Week 0)

8. Change from Baseline in FACIT-F at Week 52

9. Proportion of subjects with clinical remission per PROs and endoscopic remission at Week 52

10. Proportion of subjects with CD-related hospitalizations during the 52 Week double-blind maintenance period.

11. Proportion of subjects with resolution of extra-intestinal manifestations (EIMs) at Week 52, in subjects with EIMs at Baseline.

Sub-study 2: No Secondary Endpoints

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

This study has been transitioned to CTIS with ID 2023-504951-29-00 check the CTIS register for the current data.

The objective of Substudy 1 (randomized, double-blind, placebo-controlled maintenance) is to evaluate the efficacy and safety of two doses of upadacitinib versus placebo as maintenance therapy in subjects with moderately to severely active Crohn's disease (CD) who responded to upadacitinib induction treatment in Studies M14-431 or M14-433. The objective of Substudy 2 (long-term extension [LTE]) is to evaluate safety and efficacy of long-term administration of upadacitinib in subjects with moderately to severely active CD who participated in the Phase 3 upadacitinib induction and maintenance studies.

Study design

This is a phase 3, multicenter, randomized, double-blind, placebo-controlled maintenance and long-term extension 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. Subject 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 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 M14-430 will further evaluate the benefit to risk profile of upadacitinib as maintenance therapy in subjects with CD who have inadequately responded are intolerant to conventional or biologic therapies and have responded to upadacitinib induction treatment. 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
AbbVie B.V.

Wegalaan 9
Hoofddorp 2132JD
NL
Scientific
AbbVie B.V.

Wegalaan 9
Hoofddorp 2132JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

For Substudy 1:
- Subject achieved clinical response in Study M14-431 or Study M14-433.
- Subject completed Week 12 (in subjects who achieve response at Week 12) or Week 24 (in subjects who achieve response at Week 24) visit and procedures in Study M14-431 or Study M14-433. The final endoscopy for Studies M14-431 or M14-433 may be missing, if the endoscopy cannot be performed during the COVID-19 pandemic.
Note: Subjects completing Part 3/Cohort 3 of Study M14-431, who received open-label Extended Treatment, should enroll in Substudy 2.

For Substudy 2:
- Subject completed Week 52 of the maintenance period of Study M14-430 (Substudy 1).Completion includes the Week 52 endoscopy of Substudy 1. The Week 52 endoscopy may be missing, if the endoscopy cannot be performed during the COVID-19 pandemic or any state of emergency or pandemic situation.
- Subject achieved clinical response at Week 24 and completed Week 24 visit and procedures in Part 3/Cohort 3 of Study M14-431.

Exclusion criteria

For Sub-studies 1 and 2:
- Participant is considered by the investigator, for any reason, to be an unsuitable candidate for the study.
- Participant who has a known hypersensitivity to upadacitinib or its excipients, or had an adverse event during Study M14-431 or Substudy 1 or 2 of Study M14-430 that in the investigator's judgment makes the subject unsuitable for this study.
- Participant at the final visit of M14-431 or M14-433 with any active or chronic recurring infections based on the investigator's assessment that makes the subject an unsuitable candidate for the study. Subjects with ongoing infections undergoing treatment may be enrolled BUT NOT dosed until the infection treatment has been completed and the infection is cured, based on the investigator's assessment.
- Participants with high grade colonic dysplasia or malignancy diagnosed at the endoscopy performed at the final visit of Study M14-431, M14-433, or Substudy 1 or 2 of Study M14-430 (Week 52).

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):	23-10-2018
Enrollment:	29
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:	28-11-2018
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:	17-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2019
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:	02-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	26-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2019
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:	16-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-05-2020
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:	20-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2021
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:	13-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	11-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-01-2023
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:	27-02-2023
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:	01-03-2023
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:	15-04-2023
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:	22-06-2023
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

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	CTIS2023-504951-29-00
EudraCT	EUCTR2017-001225-41-NL
ClinicalTrials.gov	NCT03345823
CCMO	NL62828.018.18