A Phase 2, Multicenter, Open-Label Extension (OLE) Study to Observe the Long-Term Efficacy, Safety, and Tolerability of Repeated Administration of Upadacitinib (ABT-494) in Subjects with Crohn's Disease

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This study has been transitioned to CTIS with ID 2024-510727-19-00 check the CTIS register for the current data. The primary objective of this study is to observe the long-term efficacy, safety, and tolerability of repeated administration of...

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

Summary

ID

NL-OMON50581

Source
ToetsingOnline

Brief title
M14-327

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
chronic inflammation of the intestine, regional enteritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Crohn's Disease, Long-Term, Open-Label Extension (OLE), Upadacitinib

Outcome measures

Primary outcome

• Proportion of subjects achieving Remission at Week 0 (Week 52 of Study

M13-740), Month 12, 24, 36, 48, 60, 72, 84, and 96

• Proportion of subjects achieving Response at Week 0 (Week 52 of Study

M13-740), Month 12, 24, 36, 48, 60, 72, 84, and 96

• Proportion of subjects in remission at week 0 who maintain remission at Month

12, 24, 36, 48, 60, 72, 84, and 96

Secondary outcome

• Proportion of subjects achieving Clinical remission over time

• Proportion of subjects achieving Clinical response over time

• Proportion of subjects achieving Endoscopic remission at Week 0 (Week 52 of

Study M13-740), Month 12, 24, 36, 48, 60, 72, 84, and 96

• Proportion of subjects achieving Endoscopic response at Week 0 (Week 52 of

Study M13-740), Month 12, 24, 36, 48, 60, 72, 84, and 96

• Proportion of subjects achieving CDAI remission over time

• Proportion of subjects achieving CDAI response over time

• Proportion of subjects achieving IBDQ remission over time

• Proportion of subjects achieving IBDQ response over time

• Proportion of subjects in Remission, and hs-CRP < 5 mg/L, and fecal

calprotectin < 250 µg/g at Week 0 (Week 52 of Study M13-740), Month 12, 24, 36,

48, 60, 72, 84, and 96

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 is associated with significant morbidity (including abdominal pain, diarrhea, weight lost/malnutrition and gastrointestinal fistulas/strictures/abscesses) related to the underlying inflammation. 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 are usually treated with conventional pharmacologic interventions, which include corticosteroids and immunomodulatory agents. Adverse events (AEs) associated with short-term use of corticosteroids include acne, moon face, edema, skin striae, glucose intolerance, and sleep/mood disturbances; potential AEs observed with longer term use (usually 12 weeks or longer but sometimes shorter durations) include posterior subcapsular cataracts, osteoporosis, osteonecrosis of the femoral head, myopathy, and susceptibility to infection.

Patients who do not respond to conventional therapies may be treated with biologics, such as anti-TNF α therapies. Despite the beneficial results achieved with the available anti-TNF α agents, approximately 40% of patients who receive them for the first time do not have a clinically meaningful response (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). Clearly, the medical need for additional therapeutic options in CD for patients with inadequate response to or intolerance to conventional therapies and anti-TNF α agents remains.

Although the pathogenesis of CD is not completely understood, the imbalance between anti-inflammatory and pro-inflammatory cytokines in the mucosal immune system is thought to play an important role in CD. Targeting the JAK (Janus

activated kinase) signaling pathway for autoimmune diseases, such as RA and CD, is well-supported by the involvement of various pro-inflammatory cytokines that signal via JAK pathways in the pathogenesis of these immune-related disorders.

Upadacitinib (ABT-494) is a novel JAK1 inhibitor being developed for the treatment of adult patients with inflammatory diseases. Previous studies with Upadacitinib (ABT-494) have shown an acceptable safety and tolerability profile and this is being further assessed in a phase 2 study for patients with Crohn*s disease. The current open-label extension study will allow the collection of long-term safety data to better assess the risk to benefit profile of Upadacitinib (ABT-494).

Study objective

This study has been transitioned to CTIS with ID 2024-510727-19-00 check the CTIS register for the current data.

The primary objective of this study is to observe the long-term efficacy, safety, and tolerability of repeated administration of Upadacitinib (ABT-494) in subjects with Crohn's disease (CD) who completed Study M13-740.

Study design

This is an open-label, multi-center, interventional, phase 2 extension study.

Intervention

All patients receive Upadacitinib (ABT-494) tablets (oral) once a day, until end of study or discontinuation.

Study burden and risks

Upadacitinib (ABT-494) is a novel JAK1 selective inhibitor with minimal inhibitory effects on JAK2 and JAK3, which could potentially minimize some of the reported safety concerns with non-selective JAK inhibition which are thought to be mediated by inhibition of JAK2 and JAK3 signaling pathways. In a previous Upadacitinib (ABT-494) study with healthy volunteers no serious or fatal adverse events were reported. Reported adverse events (AEs) were considered mild (Grade 1) in severity and were mostly reported to have a reasonable possibility of being related to the study drug. The most common reported AEs were: headache, abdominal pain, diarrhea and nasopharyngitis.

Study M13-740, an ongoing Phase 2 double-blind randomized controlled study in CD subjects with multiple doses of Upadacitinib (ABT-494) is based on the following supportive findings: 1) demonstrated improved potency of Upadacitinib (ABT-494) versus tofacitinib in preclinical models of inflammation; 2)

confirmed JAK1 selectivity of Upadacitinib (ABT-494) in both preclinical and clinical settings; 3) acceptable preclinical toxicological findings in chronic toxicity studies in two species; 4) acceptable safety and tolerability profile of Upadacitinib (ABT-494) in healthy volunteers and 5) evidence that JAK inhibition in preclinical models of inflammatory bowel disease results in clinical and endoscopic improvement.

The possible clinical improvement outweighs the risks mentioned above and the limited additional study activities over a period of 96 months (doctor visits, blood drawings, questionnaires and medication diary). Additionally, patients are closely monitored for any AEs and their relationship to the study drug will be evaluated by the investigator, documented and analysed.

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

Subject must have completed Study M13-740 through Week 52.

Exclusion criteria

• For any reason subject is considered by the investigator to be an unsuitable candidate, • Female subject with a positive pregnancy test at Baseline or who is considering becoming pregnant during the study. , • Subject is not in compliance with prior and concomitant medication requirements and procedures throughout Study M13-740.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-02-2017
Enrollment:	6
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	06-06-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2019
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:	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:	05-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-03-2020
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:	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:	20-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-12-2020
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:	17-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2022
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:	05-12-2022
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:	11-06-2023

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:	22-08-2023
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:	19-12-2023
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:	07-02-2024
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	CTIS2024-510727-19-00
EudraCT	EUCTR2015-003759-23-NL
CCMO	NL56515.018.16