A phase 3 multicenter, long-term extension study to evaluate the long-term safety and efficacy of Upadacitinib (ABT-494) in subjects with ulcerative colitis (UC).

Published: 22-08-2016
Last updated: 08-02-2025

This study has been transitioned to CTIS with ID 2023-505699-31-00 check the CTIS register for the current data. To evaluate the Long-Term Safety and Efficacy of upadacitinib.

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

Summary

ID

NL-OMON54675

Source
ToetsingOnline

Brief title
M14-533

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
chronic bowel inflammation, ulcerative colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ABT-494, Long-Term Extension, Ulcerative Colitis, Upadacitinib

Outcome measures

Primary outcome

The primary endpoint of the study is to evaluate the long-term safety and tolerability of upadacitinib through the assessment of the incidence of treatment-emergent adverse events, changes in vital signs, physical examination results, and clinical laboratory data.

Secondary outcome

The clinical remission or response will be evaluated using the Mayo Scoring System for Assessment of Ulcerative Colitis Activity (Full Mayo score), Adapted Mayo score (Full Mayo score excluding Physician's Global Assessment), or Partial Mayo score (Full Mayo score excluding endoscopic subscore).

Study description

Background summary

Ulcerative colitis (UC) is a chronic, relapsing inflammatory disease of the large intestine characterized by inflammation and ulceration of mainly the mucosal and occasionally submucosal intestinal layers. The hallmark clinical symptoms include bloody diarrhea associated with rectal urgency and tenesmus. The most severe intestinal manifestations of UC are toxic megacolon and perforation. Patients with UC are at an increased risk for colon cancer, and the risk increases with the duration of disease as well as extent of colon affected by the disease. The aim of medical treatment in UC is to control inflammation and reduce symptoms. Available pharmaceutical therapies are

limited, do not always completely abate the inflammatory process, and may have significant adverse effects. Therapies for mild to moderate active UC include 5-aminosalicylic acid derivatives and immunosuppressants. Corticosteroids are used in patients with more severe symptoms but are not useful for longer term therapy. The frequency and severity of corticosteroid toxicities are significant, including infections, emotional and psychiatric disturbances, skin injury, and metabolic bone disease. Patients with moderate to severe symptoms may derive some benefits from immunomodulatory agents, however, the use of these agents is limited as induction treatment due to a slow onset of action (3 to 6 months) and as maintenance therapy due to adverse events (AEs), including bone marrow suppression, infections, hepatotoxicity, pancreatitis, and malignancies. Biological agents targeting specific immunological pathways have been evaluated for their therapeutic effect in treating patients with UC as well, such as anti-tumor necrosis factor (TNF) agents. Anti-TNF therapies are an effective treatment for patients who are steroid refractory or steroid dependent, who had inadequate response to a thiopurine, or who are intolerant to these medications. Potential risks with anti-TNF therapies include infusion or injection site reactions, serious infections, lymphoma, heart failure, lupus-like syndromes, and demyelinating conditions. Despite the beneficial results achieved with the available biologic agents, only 17% to 45% of patients who receive them are able to achieve clinical remission. Thus, there remains a clear medical need for additional therapeutic options in UC for patients with inadequate response to or intolerance to conventional therapies and biologic therapies. The Janus kinases or JAKs are a family of intracellular tyrosinekinases that function as dimers in the signaling process of many cytokine receptors. The JAKs play a critical role in both innate and adaptive immunity, making them attractive targets for the treatment of inflammatory diseases. Targeting the Janus activated kinase (JAK) signaling pathway for autoimmune diseases is supported by the involvement of various pro-inflammatory cytokines that signal via JAK pathways in the pathogenesis of these immune-related disorders. Upadacitinib is a novel selective JAK1 inhibitor. JAK1 inhibition blocks the signaling of many important pro-inflammatory cytokines.

Study objective

This study has been transitioned to CTIS with ID 2023-505699-31-00 check the CTIS register for the current data.

To evaluate the Long-Term Safety and Efficacy of upadacitinib.

Study design

This is a Phase 3, multicenter, long-term extension (LTE) study which comprises an up to 288-week follow up period (with the option of continued treatment dependent on country specific regulatory approval and local requirements)

designed to evaluate the long-term safety and efficacy of upadacitinib

Intervention

All subjects receive upadacitinib tablets (oral) once a day, until end of study or discontinuation.

Study burden and risks

Upadacitinib 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. Upadacitinib was tested in two studies in patients with RA. Upadacitinib was generally well-tolerated and the types and frequencies of side-effects were typical of patients treated with traditional RA medications. The most common reported AEs were: headache, upper chest infection, common cold, back pain, diarrhea, and cough. This Phase 3 long-term extension Study M14-533 will assess the long-term safety and efficacy of upadacitinib in subjects with UC who participated in the Phase 2b/3 Study M14-234 or Phase 3 Study M14-675. The possible clinical improvement outweighs the risks mentioned above as well as the limited additional study activities over a period of 288 weeks (doctor visits, blood drawings, questionnaires and medication diary). Additionally, subjects are closely monitored for any AEs and their relationship to the study drug will be evaluated by the investigator, documented and analyzed.

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. Subject has not responded at the end of the induction period (Week 8) in study M14-234 (substudie 1), who has been an inadequate responder during the maintenance period of study M14-234 (Substudy 3), or who has responded and successfully completed study M14-234.

During the COVID-19 pandemic, for subjects with missing endoscopy due to the COVID-19 pandemic in studies M14-234 SS2, SS3 and M14-675 those following subjects may be enrolled if the below criteria is met:
* Subjects who achieved clinical response defined by Partial Adapted Mayo Score at Week 8 of Studies M14-234 SS2 and M14-675
* Subjects who achieved clinical response defined by Partial Adapted Mayo Score at Week 16 in the extended treatment period of Studies M14-234 SS2 and M14-675
Note: If endoscopy is missing at Week 8 but can be performed at Week 16, Week 16 endoscopy should be performed. However, the status of clinical response will be defined by Partial Adapted Mayo Score and clinical responders may enter Study M14-533 Cohort 1.
* Subjects who have completed the 52-week treatment in Study M14-234 SS3 if the PI considers it is safe to continue based on phone/video call, subject's medical history and findings from the last endoscopy.

2. Women of childbearing potential (refer to section 5.2.4 of the protocol) must have a negative urine pregnancy test at Week 0 visit.

3. If female, subject must meet the contraception criteria.

4. Subject is judged to be in otherwise good health as determined by the principal investigator based upon clinical evaluations performed during the preceding studies.

5. Must be able and willing to give written informed consent and to comply with the requirements of this study protocol.

Exclusion criteria

1. For any reason subject is considered by the investigator to be an unsuitable candidate.

2. Female subject with a positive pregnancy test at Baseline (final visit of the preceding studies) or who is considering becoming pregnant during the study and within 30 days after the last dose of study drug.

3. Known hypersensitivity to upadacitinib or its excipients or had any adverse event (AE) during the preceding studies, that in the investigator's judgment makes the participant unsuitable for this study

4. Subject with an active or recurrent infection that based on the investigator's clinical assessment makes the subject an unsuitable candidate for the study. Subjects with ongoing infections undergoing treatment may be enrolled BUT NOT dosed until the infection has been successfully treated.

5. Current evidence of active tuberculosis; Current evidence of latent tuberculosis and for any reason the subject cannot take full course of TB prophylaxis treatment

6. Subject with a poorly controlled medical condition, such as uncontrolled diabetes, unstable ischemic heart disease, moderate or severe congestive heart failure, recent cerebrovascular accidents and any other condition which, in the opinion of the investigator or sponsor, would put the subject at risk by participation in this study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-06-2017
Enrollment:	40
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	22-08-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	24-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	12-09-2018
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:	22-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2019
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:	24-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2019
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:	20-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2020
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:	26-11-2020
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:	07-07-2021
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:	11-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2022
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:	08-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	25-04-2023
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:	13-05-2023
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:	18-10-2023
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	CTIS2023-505699-31-00
EudraCT	EUCTR2016-000674-38-NL
CCMO	NL58325.018.16