A Phase 3, Randomized, Active-Controlled, Double Blind Study Comparing Upadacitinib (ABT 494) to Abatacept in Subjects with Moderately to Severely Active Rheumatoid Arthritis with Inadequate Response or Intolerance to Biologic DMARDs (bDMARDs) on Stable Conventional Synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs)

Published: 18-04-2017
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Main objective:1. To compare the safety and efficacy of upadacitinib 15 mg once daily (QD) versus abatacept intravenous (IV) for the treatment of signs and symptoms of rheumatoid arthritis (RA) in bDMARD-inadequate response (bDMARD-IR) or bDMARD-...

Ethical review	Approved WMO
Status	Completed
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON53110

Source
ToetsingOnline

Brief title
M15-925

Condition

- Autoimmune disorders
- Joint disorders

Synonym
Rheumatoid Arthritis and Rheumatism

Research involving
Human

Sponsors and support

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

Intervention

Keyword: DMARDs, JAK-inhibitor, Rheumatoid arthritis

Outcome measures

Primary outcome

Change from baseline in DAS28 (CRP) (non-inferiority).

Secondary outcome

Secondary objectives:

1. Change from baseline in DAS28 (CRP) at Week 12 (superiority);

2. Proportion of subjects achieving Clinical Remission (CR) at Week 12

(superiority)

Study description

Background summary

Despite major progress in the treatment of RA, there still remains a large unmet medical need, as only a small percentage of RA patients reach or maintain

a status of LDA or CR over time or need to discontinue due to safety or tolerability issues. Novel therapies are therefore needed to complement the available interventions to address the unmet need.

Evidence suggests that inhibition of Janus kinase (JAK)-mediated pathways is a promising approach for the treatment of patients with this chronic disease. AbbVie is developing a small molecule inhibitor of JAK, upadacitinib, that may address the current needs.
Previous studies with both upadacitinib and abatacept have demonstrated robust and statistically significant improvement in disease activity at 12 week compared to placebo. This study differs from other upadacitinib studies as it is the first study to evaluate the safety and efficacy of upadacitinib vs. abatacept in subjects with inadequate response to or intolerance to bDMARD treatment.

Study objective

Main objective:
1. To compare the safety and efficacy of upadacitinib 15 mg once daily (QD) versus abatacept intravenous (IV) for the treatment of signs and symptoms of rheumatoid arthritis (RA) in bDMARD-inadequate response (bDMARD-IR) or bDMARD-intolerant subjects with moderately to severely active RA.

2. To evaluate the long-term safety, tolerability, and efficacy of upadacitinib 15 mg QD in subjects with RA.

Secondary objectives:
1. Change from baseline in DAS28 (CRP) at Week 12 (superiority);

2. Proportion of subjects achieving Clinical Remission (CR) at Week 12 (superiority)

Study design

A 24-week randomized, double-blind, parallel-group, active-controlled treatment period followed by an open label long-term extension period

Intervention

Subjects who meet eligibility criteria will be randomized in a 1:1 ratio to one of two treatment groups:
• Group 1: upadacitinib tablet QD, (Period 1)
• Group 2: Abatacept IV at Day 1, Weeks 2, 4, 8, 12, 16 and 20 (Period 1)

Subjects who complete the Week 24 visit (end of Period 1) will enter the open-label long term extension portion of the study, Period 2 (192 weeks).

Subjects who are assigned to upadacitinib treatment group in Period 1 will continue to receive upadacitinib QD per original randomization assignment. Subjects who are assigned to abatacept IV in Period 1 will be switched to receive upadacitinib 15 mg QD.

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 frequent in period 1. Subjects will take daily tablets (placebo or upadacitinib) and receive an IV infusion of abatacept or placebo. During these visits study procedures will be performed among which blood sampling and questionnaires. Subject will also be tested for TB, significant heart conditions, pregnancy, HCV/HBV and HIV. Subject will also complete a daily diary.

Subjects will either receive upadacitinib or abatacept during the study. The most frequently reported AEs (>= 5%) in the upadacitinib treated subjects were urinary tract infection, headache, upper respiratory tract infection, and nausea. Safety monitoring will be done during the study.

Taken together, the safety and efficacy data from the Phase 2 program show a favorable benefit:risk profile for upadacitinib that supports further development of upadacitinib in Phase 3 in subjects with RA.

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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. Adult male or female, at least 18 years old., 2. Diagnosis of RA for >= 3 months., 3. Subjects have been treated for >= 3 months with >= 1 bDMARD therapy, but continue to exhibit active RA or had to discontinue due to intolerability or toxicity, irrespective of treatment duration and have never received abatacept prior to the first dose of study drug., 4. Subjects have been receiving csDMARD therapy >= 3 months and on a stable dose for >= 4 weeks prior to the first dose of study drug. The following csDMARDs are allowed: MTX, sulfasalazine, hydroxychloroquine, chloroquine, and leflunomide. A combination of up to two background csDMARDs is allowed except the combination of MTX and leflunomide., 5. Meets the following criteria: >= 6 swollen joints (based on 66 joint counts) and >= 6 tender joints (based on 68 joint counts) at Screening and Baseline Visits and hsCRP >= 3 mg/L at Screening.

Exclusion criteria

1. Prior exposure to any Janus kinase (JAK) inhibitor (including but not limited to tofacitinib, baricitinib, and filgotinib). , 2. Prior exposure to abatacept, 3. History of inflammatory joint disease other than RA. Current diagnosis of secondary Sjogren's Syndrome is permitted.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-02-2018
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Orencia
Generic name:	Abatacept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	upadacitinib
Generic name:	upadacitinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-04-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2017
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-05-2018
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2019
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:	03-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-11-2019
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2020
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:	22-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-06-2021
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:	03-08-2022
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:	19-12-2022
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	EUCTR2016-000933-37-NL
ClinicalTrials.gov	NCT03086343
CCMO	NL58599.048.16

Study results

Date completed:	05-04-2023
Results posted:	31-05-2024

First publication
07-05-2024

URL result
URL

Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File