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

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Period 1: The first objective, of period 1, is to compare the safety and efficacy of ABT-494 30 mg (QD) and 15 mg QD versus placebo on a background of csDMARD(s) for the treatment of signs and symptoms of rheumatoid arthritis (RA) in bDMARD-…

Ethical review	Not approved
Status	Will not start
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON43876

Source
ToetsingOnline

Brief title
M13-542 (Bio-IR)

Condition

- Autoimmune disorders
- Joint disorders

Synonym
'Rheumatoid Arthitis' and 'Rheumatism'

Research involving
Human

Sponsors and support

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

Intervention

Keyword: JAK-inhibitors, Placebo, Rheumatoid Arthritis

Outcome measures

Primary outcome

The primary endpoint is the proportion of subjects achieving ACR20 response

(US/FDA regulatory purposes) or the proportion of subjects achieving LDA

(EU/EMA regulatory purposes) at Week 12.

Secondary outcome

Secondary endpoints at week 12 are:

1. Change from baseline in DAS28 (CRP);

2. ACR20 response rate;

3. ACR50 response rate;

4. Change from baseline in HAQ-DI;

5. ACR70 response rate;

6. Change from baseline in SF-36 PCS;

7. ACR20 response rate at week 1.

Additional endpoints at all visits are:

* Change from baseline in individual components of ACR response;

* ACR20/50/70 response rates;

* Change from baseline in DAS28 (CRP) and DAS28 (erythrocyte sedimentation rate [ESR]);

* Change from baseline in morning stiffness (severity and duration);

* Proportion of subjects achieving LDA and proportion of subjects achieving CR based on DAS28 (CRP), DAS28 (ESR), Simplified Disease Activity Index (SDAI), and CDAI criteria.

Additional endpoints (at Weeks 4, 12, and 24) are:

* Change from baseline in EQ-5D-5L;

* Change from baseline in ISI (sleep);

* Change from baseline in SF-36.

Assessments to evaluate efficacy of treatment in Period 2 will be analyzed for above-mentioned measures at Weeks 36, 48 and every 12 weeks thereafter until completion of the study.

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease characterized by inflammation of the articular synovial membrane. The hallmark feature of patients affected by RA is an inflammatory process manifested by persistent symmetric polyarthritis of synovial joints. Early therapy with disease-modifying antirheumatic drugs (DMARDs) is the standard of care, although a significant proportion of patients either do not achieve disease

remission or become refractory to available therapies as the disease progresses. Novel therapies are therefore required to complement the available interventions to address the unmet need in the treatment of patients with RA. 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, ABT-494, that may address the current medical needs.

Study objective

Period 1:
The first objective, of period 1, is to compare the safety and efficacy of ABT-494 30 mg (QD) and 15 mg QD versus placebo on a background of csDMARD(s) 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.

Periode 2:
The objective of this study in periode 2, is to evaluate the long-term safety, tolerability, and efficacy of ABT-494 30 mg QD and 15 mg QD in subjects with RA who have completed Period 1.

Study design

This is a phase 3, multicenter study that includes to periods. Period 1 is a randomized, double-blind, placebo-controlled treatment period of 24 weeks. Period 2 is a blinded long-term extension period for subjects who completed period 1.

Subjects will be randomized in a 2:2:1:1 ratio to one of 4 treatment groups:
- Group 1: ABT-494 30 mg QD (week 1 to 12) --> ABT-494 30 mg QD (week 12 and thereafter)
- Group 2: ABT-494 15 mg QD (week 1 to 12) --> ABT-494 15 mg QD (week 12 and thereafter)
- Group 3: Placebo (week 1 to 12) --> ABT-494 30 mg QD (week 12 and thereafter)
- Group 4: Placebo (week 1 to 12) --> ABT-494 15 mg QD (week 12 and thereafter)

The study will be conducted in approximately 300 research centers and approximately 250 subjects will be enrolled.

Intervention

Subjects who are randomized in the ABT-494 treatment groups will start their dose ABT-494 30 mg QD or ABT-494 15 mg QD orally at Baseline and must take their oral dose of medication once daily for 12 weeks. Subjects who are randomized in the Placebo treatment groups will receive matching placebo for

ABT-494 to remain the blind and must take their oral dose of medication oral once daily for 12 weeks. From week 12 and thereafter, subjects who are assigned to the Placebo group will be switched to receive ABT-494 30 mg QD or ABT-494 15 mg QD.

Subjects who complete the week 24 visit (end of period 1) will enter the blinded long term extension portion of the study (period 2). Subjects who are assigned to ABT-494 treatment groups in period 1 will continue to receive ABT-494 15 mg QD or 30 mg QD per original randomization assignment in a blinded manner. Subjects who are assigned to placebo for the first 12 weeks of period 1 and subsequently switched to receive ABT-494 15 mg or 30 mg QD per pre-specified randomization assignments at week 12, will continue to receive the same dose of ABT-494 per original randomization assignment in a blinded manner.

Subjects who do not achieve CDAI * 10 at Week 24 should have background medication(s) adjusted or initiated after assessments for Week 24 have been completed.

Study burden and risks

Subjects participating in this study are required to come to all scheduled visits and complete the procedures, as described in section E.4. Risks of participating in this study are: - higher dose and/or frequency of drug administration - extra time - (extra) procedures) - come to all scheduled visits -adverse events (described in section E.9) - discomfort of tests that will be conducted during study.

Contacts

Public
AbbVie B.V.

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

Wegalaan 9
Hoofddorp 2132 JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Adult male or female, at least 18 years old.;* Diagnosis of RA for * 3 months.;* 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 prior to the first dose of study drug. ;* 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.;* 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.

Exclusion criteria

* Prior exposure to any Janus kinase (JAK) inhibitor (including but not limited to tofacitinib, baricitinib, and filgotinib).;* History of inflammatory joint disease other than RA. History 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:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	ABT-494
Generic name:	ABT-494

Ethics review

Approved WMO Date:	15-03-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-07-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Not approved Date:	11-07-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2015-003335-35-NL
ClinicalTrials.gov	NCT02706847
CCMO	NL54437.091.16