A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study to investigate the Safety and Efficacy of ABT-494 Given with Methotrexate (MTX) in Subjects with Moderately to Severely Active Rheumatoid Arthritis (RA) Who Have Had an Inadequate Response or Intolerance to Anti-TNF Biologic Therapy

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON40747

Source
ToetsingOnline

Brief title
M13-550, ABT-494

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
rheumatic diseases, Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie Deutschland GmbH & Co. KG
Source(s) of monetary or material Support: Industry

Intervention

Keyword: ABT-494, M13-550, phase 2, Rheumatoid Arthritis (RA)

Outcome measures

Primary outcome

Efficacy:

The primary endpoint of this study is the ACR20 response rate at Week 12. ACR20 response rate will be determined based on 20% or greater improvement in Tender Joint Count (TJC) and Swollen Joint Count (SJC) and >= 3 of the 5 measures of Patient's Assessment of Pain (VAS), Patient's Global Assessment of Disease Activity, Physician's Global Assessment of Disease Activity, Patient's Assessment of Disability (HAQ-DI) or hsCRP. The secondary endpoints of this study are ACR50/70 response rates at Week 12, the proportion of subjects achieving low disease activity (LDA) (2.6 <= DAS28 [CRP] < 3.2) or clinical remission (CR) (DAS28 [CRP] < 2.6), and the proportion of subjects achieving CR (DAS28 [CRP] < 2.6) at Week 12.

Pharmacokinetics:

For all subjects, PK trough samples will be collected at each visit beginning

on Day 1 (Baseline) through Week 12. For 30% of subjects, in addition to trough PK samples at each visit, PK samples will be collected on Day 1 (Baseline) and Week 8 at 1, 2, and 3 hours post-morning dose.

Safety:

Safety evaluations include adverse event monitoring, physical examinations, vital sign measurements, electrocardiogram, and clinical laboratory testing (hematology, chemistry, and urinalysis) as a measure of safety and tolerability. Toxicity management guidelines are provided in the protocol.

Secondary outcome

Secondary Efficacy Variables:

* ACR50 and ACR70 response rates at Week 12

* Proportion of subjects achieving low disease activity (LDA) (2.6 <= DAS28 [CRP] < 3.2) or clinical remission (CR) (DAS28 [CRP] < 2.6) at Week 12.

* Proportion of subjects achieving CR based on DAS28 [CRP] < 2.6 at Week 12.

Study description

Background summary

ABT-494 is being developed for the treatment of adult patients with moderate to severe active rheumatoid arthritis (RA). The enhanced selectivity of ABT-494 may offer an improved benefit:risk profile in patients with RA.

Study objective

The primary objective is to compare the safety and efficacy of multiple doses of ABT-494 versus placebo in moderately to severely active RA subjects on stable background MTX therapy with inadequate response or intolerance to

anti-TNF biologic therapy.

Study design

This is a Phase 2, randomized, double-blind, parallel-group, placebo-controlled multicenter study comparing the safety and efficacy of multiple twice daily (BID) doses of ABT-494 versus placebo administered for 12 weeks in subjects with moderately to severely active RA who have shown an inadequate response or intolerance to anti-TNF biologic treatment(s).

Intervention

Subjects will be randomized in a 1:1:1:1:1 fashion to one of 4 doses of ABT-494 or placebo, all administered with stable background MTX therapy.

The following are the treatment groups:
Group 1: take twice a day one capsule of ABT-494 3 mg BID
Group 2: take twice a day one capsule of ABT-494 6 mg BID
Group 3: take twice a day one capsule of ABT-494 12 mg BID
Group 4: take twice a day one capsule of ABT-494 18 mg BID
Group 5: take twice a day one capsule of Placebo BID

Study burden and risks

The prevalence of Rheumatoid arthritis (RA) in the general population is approximately 1%, and increases with age in both genders, with women being more prone for developing RA than men. RA subjects who inadequately responded to or are unable to tolerate an anti-TNF therapy are a subgroup of patients with significant unmet medical need. We would like to us ABT-494 for this patient population. The information that is obtained during this study is useful scientifically and thus be helpful to others with the same condition in the future.

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. Adult male or female, at least 18 years old.;2. Diagnosed with RA based on either the 1987-revised American College of Rheumatology (ACR)
classification criteria or the 2010 American College of Rheumatology/European League against
Rheumatism (ACR/EULAR) criteria for >= 3 months.;3. Subjects must have been receiving oral or parenteral MTX therapy >= 3 months and on a stable
prescription of 7.5 to 25 mg/week for at least 4 weeks prior to initiating the study drug. Subjects
should also be on a stable dose of folic acid (or equivalent) for at least 4 weeks prior to initiating the study drug. Subjects should continue with their stable doses of MTX and folic acid throughout the study.;4. Subjects have been treated with 1 or 2 anti-TNF biologics for >= 3 months but continue to exhibit
active RA, or had to discontinue due to intolerability or toxicity. In addition, subjects may have
received up to 1 non-anti-TNF biologic (e.g., abatacept, rituximab, anakinra, or tocilizumab) prior
to Screening.;5. Have active RA as defined by the following minimum disease activity criteria:
• >= 6 swollen joints (based on 66 joint counts) at Screening and Baseline Visits.
• >= 6 tender joints (based on 68 joint counts) at Screening and Baseline Visits.
• hs-CRP > Upper Limit of Normal (ULN) OR positive for both rheumatoid factor and anti-CCP antibody.

Exclusion criteria

A subject will be excluded from the study if he/she meets any of the following criteria:
1. Prior exposure to JAK inhibitor (e.g., tofacitinib, baricitinib).
2. Receipt of any investigational drug of chemical or biologic nature within a minimum of 30 days or 5 half-lives of the drug (whichever is longer) prior to initiating the study drug.
3. Current or expected need of other immunosuppressant medications, except MTX. Use of oral intake of > 10 mg prednisone/day or equivalent corticosteroid therapy.
4. Screening laboratory values meeting the following criteria:
• Serum aspartate transaminase (AST) or alanine transaminase (ALT) > 1.5 × ULN
• Estimated glomerular filtration rate (eGRF) by simplified 4-variable Modification of Diet in Renal Disease (MDRD) formula < 40 mL/min/1.73 m2
• Total white blood cell count (WBC) < 3,000/µL
• Absolute neutrophil count (ANC) < 1,200 /µL
• Platelet count < 100,000/µL
• Absolute lymphocytes count < 750/µL
• Hemoglobin < 9 gm/dL

Study design

Design

Study phase:	2
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:	12
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	24-02-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	16-01-2015
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	EUCTR2013-002358-57-NL
ClinicalTrials.gov	NCT01960855
CCMO	NL47690.018.14