Phase 2 Study, Multicenter, Open-Label Extension (OLE) Study in Rheumatoid Arthritis Subjects Who Have Completed a Preceding Phase 2 Randomized Controlled Trial (RCT) with ABT-494

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To evaluate the long-term safety, tolerability, and efficacy of ABT-494 in RA subjects who have completed Study M13-550 or Study M13-537 Phase 2 RCT with ABT-494.

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

Summary

ID

NL-OMON41802

Source
ToetsingOnline

Brief title
M13-538, 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, M13-538, Phase 2, Rheumatoid Arthritis

Outcome measures

Primary outcome

Efficacy:

ACR20/50/70 response rates at Weeks 6, 12, 24, 36, 48, 60, 72, 84 and 96 will be evaluated based on 20/50/70% improvement in TJC, 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, Health Assessment Questionnaire Disability Index (HAQ-DI), and hsCRP.

Change from Baseline in individual ACR components at Weeks 6, 12, 24, 36, 48, 60, 72, 84 and 96 will also be evaluated: TJC, SJC, Patient's Assessment of Pain (VAS), Patient's Global Assessment of Disease Activity, Physician's Global Assessment of Disease Activity, Health Assessment Questionnaire Disability Index (HAQ-DI), and hsCRP. Baseline data for each subject will be the data collected at the visit immediately prior to starting treatment with active ABT-494 (this visit could be in RCT or OLE).

The proportion of subjects achieving Low Disease Activity (LDA) or Clinical Remission (CR), and the proportion of subjects achieving CR will be evaluated at Weeks 6, 12, 24, 36, 48, 60, 72, 84 and 96. The criteria will be based on DAS28 [CRP] or CDAI as follows:

DAS28 [CRP] CDAI

LDA 2.6 <= to < 3.2 2.8 < to <= 10

CR < 2.6 <= 2.8

Change from Baseline in DAS28 [CRP] disease activity score, CDAI and Patient Reported Outcomes including FACIT-Fatigue Scale, RA-WIS, and EQ-5D will be analyzed at Weeks 6, 12, 24, 36, 48, 72 and 96.

Pharmacokinetic:

Individual plasma concentrations of ABT-494 will be tabulated and summarized.

Pharmacodynamic/Efficacy:

Changes from Baseline in in-vivo pharmacodynamic biomarkers and RA disease response biomarkers will be analyzed at Weeks 6, 12, 24, 36, 48, 72 and 96.

Safety:

Safety evaluations will include adverse event monitoring, physical examinations, vital sign measurements, and clinical laboratory testing (hematology, chemistry, and urinalysis). Toxicity management guidelines are included in the protocol.

Secondary outcome

N/A

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown etiology. If left untreated, RA causes damage to cartilage, bone, and adjoining tissues which ultimately leads to severe disability, impaired function, and marked reduction in the quality of life of subjects.
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 ABT-494 is a promising approach for the treatment of patients with this chronic disorder. This open-label extension study is designed to collect long-term safety, tolerability, and efficacy data.
Collecting long-term safety data is important to assess the risk to benefit profile of ABT-494. This is the first study with ABT-494 of treatment durations longer than 24 weeks.

Study objective

To evaluate the long-term safety, tolerability, and efficacy of ABT-494 in RA subjects who have completed Study M13-550 or Study M13-537 Phase 2 RCT with ABT-494.

Study design

This is a 96-week extension study to assess the long-term safety, tolerability, and efficacy of ABT-494 in RA subjects who have completed Study M13-550 or Study M13-537 RCT with ABT-494.
All eligible subjects will be assigned to ABT-494 6 mg BID immediately following the Last Visit of Study M13-550 or Study M13-537.
Subjects who are unable to tolerate 6 mg BID will be discontinued from the study.

At Week 6, if a subject fails to achieve at least 20% improvement from RCT Baseline in Tender Joint Count (TJC) and Swollen Joint Count (SJC), ABT-494 dose should be increased to 12 mg BID as long as the Investigator has no safety concerns.
After 6 weeks of treatment with ABT-494 12 mg BID the improvement in TJC and SJC will be re-assessed at next scheduled visit (Week 12).
If the subject on 12 mg BID fails to achieve at least 20% improvement in TJC and SJC from RCT Baseline the subject will be discontinued.

At Week 12, the same process will be followed.
If a subject still on 6 mg BID fails to achieve at least 20% improvement from RCT Baseline in TJC and SJC, ABT-494 dose should be increased to 12 mg BID. The improvement in TJC and SJC will be re-assessed after 6 weeks of treatment with 12 mg BID at Week 18 (an optional study visit). Subjects who fail to achieve at least 20% improvement from RCT Baseline in TJC and SJC with 12 mg BID at Week 18 will be discontinued.
After Week 12 if a subject fails to show at least 20% improvement from RCT Baseline in TJC and SJC at 2 consecutive scheduled study visits then the subject will be discontinued.

Starting at Week 6 and during any scheduled visits thereafter, ABT-494 dose may be increased from 6 mg BID to 12 mg BID if a subject fails to achieve the Low Disease Activity (LDA) status (CDAI > 10) and has no safety concerns per Investigator's judgment.
At any visit, ABT-494 dose may be decreased back to 6 mg BID per Investigator's judgment due to either an adverse event or reaching one of the protocol specific toxicity management thresholds. Dose increase back to 12 mg BID is not allowed.

Study visits will occur at BL, Weeks 6, 12, 24, 36, 48, 60, 72, 84 and 96.
Optional Study Visit at Week 18.

Intervention

Investigational Product: ABT-494 3 mg and 12 mg capsules

Doses:
6 mg BID (initial dose assignment for all subjects).
ABT-494 doses of 12 mg BID are allowed during the OLE treatment period (see above 'Study Design').

Mode of Administration: Oral

Study burden and risks

Initiation of Phase 2 studies with ABT-494 was feasible based on acceptable safety and tolerability profile of ABT-494 in single ascending dose and multiple ascending dose studies in healthy volunteers. The current open-label extension study will allow the collection of long-term safety data to better assess the risk to benefit profile of ABT-494.

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. Subjects who have completed Study M13-550 or Study M13-537 with ABT-494 and has not developed any discontinuation criteria, defined in Section 5.4.1 of that study.;2. If the subject has evidence of new latent TB infection, the subject must initiate and complete a minimum of 2 weeks (or per local guidelines, whichever is longer) of an ongoing TB prophylaxis before continuing to receive study drug.;3. If female, subject must meet one of the following criteria:;• Postmenopausal (defined as no menses for at least 1 year).;• Surgically sterile (bilateral oophorectomy or hysterectomy).;• Practicing from the time of screening until at least 30 days after the last dose of study drug at least TWO of the following methods of birth control:;- Tubal ligation;- Partner vasectomy (at least 6 months earlier) (the vasectomized male partner should be the sole partner for that female subject);- Intrauterine device;- A male condom with spermicidal jelly or cream;- Diaphragm, contraceptive sponge or cervical cap with spermicidal jelly or cream;- Hormonal contraceptives (injected, oral, transdermal or implanted methods) must have been taking at least 2 months prior to dosing;4. Male subjects must agree to follow protocol-specified pregnancy avoidance measures, including refraining from donating sperm, for up to 30 days post last dose of study drug.;5. Subjects must

voluntarily sign and date an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any screening or study specific procedures.;6. Subject is judged to be in good health as determined by the Investigator based on the results of medical history, physical examination and laboratory profile performed.

Exclusion criteria

1. Pregnant or breastfeeding female.;2. Ongoing infections at Week 0 that have NOT been successfully treated. Subjects with ongoing infections undergoing treatment may be enrolled BUT NOT dosed until the infection has been successfully treated.;3. Anticipated requirement or receipt of any live vaccine during study participation including up to 30 days after the last dose of study drug.;4. Laboratory values from the visit immediately prior to Baseline Visit meeting the following criteria:;* Serum aspartate transaminase (AST) or alanine transaminase (ALT) > 3.0 × ULN;* Estimated glomerular filtration rate by simplified 4-variable Modification of Diet in Renal Disease (MDRD) formula < 40 mL/min/1.73m2;* Total white blood cell count (WBC) < 2,000/µL;* Absolute neutrophil count (ANC) < 1,000/µL;* Platelet count < 50,000/µL;* Absolute lymphocytes count < 500/µL;* Hemoglobin < 8 gm/dL;5. Enrollment in another interventional clinical study while participating in this study.;6. Consideration by the investigator, for any reason, that the subject is an unsuitable candidate to receive study drug.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
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:	22-05-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
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	EUCTR2013-003530-33-NL

Register	ID
ClinicalTrials.gov	NCT02049138
CCMO	NL49230.018.14