A Multicenter, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Safety and Efficacy of Upadacitinib in Subjects with Active Ankylosing Spondylitis

Published: 22-08-2017
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Main objectives:1. To evaluate the efficacy of upadacitinib compared with placebo on reduction of signs and symptoms as measured by proportion of subjects who achieve an Assessment of SpondyloArthritis international Society (ASAS) 40 response at...

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

Summary

ID

NL-OMON50247

Source
ToetsingOnline

Brief title
M16-098

Condition

- Joint disorders

Synonym
Ankylosing Spondylitis, Bechterew's disease

Research involving
Human

Sponsors and support

Primary sponsor: Site Management & Monitoring
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: Ankylosing spondylitis, JAK inhibitor, Upadacitinib

Outcome measures

Primary outcome

Proportion of participants with Assessment of SpondyloArthritis international

Society (ASAS) 40 response

(It is defined as a >= 40% improvement and an absolute improvement of >= 2

units (on a scale of 0 to 10) from Baseline in at least three of the following

four domains, with no worsening at all in the remaining domain:

a. Patient's Global Assessment

b. Pain

c. Function

d. Inflammation)

Secondary outcome

1. Change from Baseline in Ankylosing Spondylitis Disease Activity Score

(ASDAS);

2. Change from Baseline in MRI Spondyloarthritis Research Consortium of Canada

(SPARCC) score (Spine);

3. Proportion of subjects with BASDAI 50 response;

4. Change from Baseline in Ankylosing Spondylitis Quality of Life (AS QoL);

5. Proportion of subjects with ASAS partial remission (PR);

6. Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI);

7. Change from Baseline in Linear Bath Ankylosing Spondylitis Metrology Index

(BASMIlin);

8. Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score

(MASES);

9. Change from Baseline in Work Productivity and Activity Impairment (WPAI);

10. Change from Baseline in ASAS Health Index (HI);

11. ASAS 20;

12. Change from Baseline in MRI Spondyloarthritis Research Consortium of Canada

(SPARCC) score Sacroiliac (SI) joints.

Study description

Background summary

Ankylosing spondylitis (AS) is a type of arthritis in which there is chronic inflammation of the joints of the spine. Despite recent advances in the treatment, there remains a significant unmet medical need as only approximately 45% to 50% of patients show an ASAS 40 response and only approximately 15% to 20% achieve a state of remission. In addition, treatment options are still limited when compared with other rheumatic diseases such as rheumatoid arthritis (RA) or Psoriatic Arthritis (PsA).

Inhibition of JAK-mediated pathways is a promising approach for the treatment of patients with chronic inflammatory diseases such as AS. AbbVie is developing a small molecule inhibitor of JAK, upadacitinib, that may address the current needs.

Study objective

Main objectives:
1. To evaluate the efficacy of upadacitinib compared with placebo on reduction of signs and symptoms as measured by proportion of subjects who achieve an Assessment of SpondyloArthritis international Society (ASAS) 40 response at Week 14 in subjects with active ankylosing spondylitis (AS) who have had an

inadequate response to at least two nonsteroidal anti-inflammatory drugs (NSAIDs) or intolerance to or a contraindication for NSAIDs, and who are biologic disease-modifying antirheumatic drug (bDMARD)-naïve.
2. To assess the safety and tolerability of upadacitinib in subjects with active AS who have had an inadequate response to at least two NSAIDs or intolerance to or a contraindication for NSAIDs, and who are bDMARD-naïve.

Secondary objective:
To evaluate the safety, tolerability, and efficacy of upadacitinib through up to 2 years of treatment in subjects who have completed Period 1.

Study design

This is a Phase 2/3 multicenter study that includes two periods. Period 1 is a 14-week randomized, double-blind, parallel-group, placebo-controlled period designed to compare the safety and efficacy of upadacitinib dose A versus placebo. Period 2 is an open-label long-term extension to evaluate the long-term safety, tolerability, and efficacy of upadacitinib Dose A QD in subjects who have completed Period 1.

Intervention

Period 1: subjects will take one tablet of upadacitinib (Dose A) or placebo once daily for 14 weeks.
Period 2: subjects will take one tablet of upadacitinib (Dose A) once daily for 194 weeks.

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 frequently. During these visits study procedures will be performed including blood sampling and questionnaires. Subject will also be tested for TB, significant heart conditions, pregnancy, HCV/HBV and HIV.
Subjects will also complete a daily diary. Women of Childbearing Potential should practice a method of birth control, during the study through at least 30 days after the last dose of study drug. If male, subjects must practice contraception during the study through at least 30 days after last dose of study drug. Additionally, male subjects must agree not to donate sperm from Study Day 1 through 30 days after the last dose of study drug.

Subjects will either receive upadacitinib or placebo during the study. The most common side effects reported during previous studies of upadacitinib were headache, upper chest infection, common cold, diarrhea and cough. An elevation of an enzyme in the blood called creatine phosphokinase (CPK, a protein released mainly from muscle cells) was observed in treated patients. Safety

monitoring will be done during the study.

The hypothesis that upadacitinib should be effective in targeting inflammation associated with AS and the lack of effectiveness of other treatments indicate that there is an acceptable rationale to conduct this study. There may or may not be benefit for study subjects but there may be benefit for future patients with ankylosing spondylitis. The subject*s condition may get better, may worsen, or may stay unchanged.

Contacts

Public
Selecteer

Wegalaan 9
Hoofddorp 2132JD
NL
Scientific
Selecteer

Wegalaan 9
Hoofddorp 2132JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male or female >= 18 years of age., 2. Subject with a clinical diagnosis of AS and meeting the modified New York Criteria for AS., 3. Subject must have

baseline disease activity as defined by having a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score >= 4 and a Patient's Assessment of Total Back Pain score >= 4 based on a 0 - 10 Numeric Rating Scale (NRS) at the Screening and Baseline Visits., 4. Subject has had an inadequate response to at least two NSAIDs over an at least 4-week period in total at maximum recommended or tolerated doses, or subject has an intolerance to or contraindication for NSAIDs as defined by the Investigator., 5. If entering the study on concomitant MTX, leflunomide, SSZ and/or hydroxychloroquine, subject must be on a stable dose of MTX (<= 25 mg/week) and/or SSZ (<= 3 g/day) and/or hydroxychloroquine (<= 400 mg/day) or leflunomide (<= 20 mg/day) for at least 28 days prior to the Baseline Visit. A combination of up to two background csDMARDs is allowed EXCEPT the combination of MTX and leflunomide., 6. If entering the study on concomitant oral corticosteroids, subject must be on a stable dose of prednisone (<= 10 mg/day), or oral corticosteroid equivalents, for at least 14 days prior to the Baseline Visit. Subject must be on stable dose(s) for at least 14 days prior to the Baseline Visit.

Exclusion criteria

1. Prior exposure to any Janus kinase (JAK) inhibitor (including but not limited to tofacitinib, baricitinib, and filgotinib)., 2. Prior exposure to any biologic therapy with a potential therapeutic impact on spondyloarthritis (SpA)., 3. Intra-articular joint injections, spinal/paraspinal injection(s), or parenteral administration of corticosteroids within 28 days prior to the Baseline Visit. Inhaled or topical corticosteroids are allowed., 4. Subject on any other DMARDs (other than those allowed), thalidomide, or apremilast within 28 days or five half-lives (whichever is longer) of the drug prior to the Baseline Visit., 5. Subject on opioid analgesics (except for combination acetaminophen/codeine or acetaminophen/hydrocodone which are allowed) or use of inhaled marijuana within 14 days prior to the Baseline Visit., 6. Subject has a history of inflammatory arthritis of different etiology other than axial SpA (including but not limited to rheumatoid arthritis (RA), psoriatic arthritis (PsA), mixed connective tissue disease, systemic lupus erythematosus, reactive arthritis, scleroderma, polymyositis, dermatomyositis, fibromyalgia), or any arthritis with onset prior to 17 years of age., 7. Laboratory values meeting the following criteria within the Screening period prior to the first dose of study drug: serum aspartate transaminase (AST) > 2 × ULN; serum alanine transaminase (ALT) > 2 × ULN; estimated glomerular filtration rate (GFR) by simplified 4-variable Modification of Diet in Renal Disease (MDRD) formula < 40 mL/min/1.73m2; hemoglobin < 10 g/dL, total white blood cell count (WBC) < 2,500/µL; absolute neutrophil count (ANC) < 1,500/µL; absolute lymphocyte count < 800/µL; and platelet count < 100,000/µL.

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:	Completed
Start date (anticipated):	18-07-2018
Enrollment:	4
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	22-08-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	05-01-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-01-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-04-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	23-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-12-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2017-000431-14-NL
CCMO	NL62813.042.17

Register	ID
Other	nog niet bekend

Study results

Date completed: 19-05-2021

Results posted: 14-02-2023

First publication
06-02-2023

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File