A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Upadacitinib in Subjects with Giant Cell Arteritis. SELECT-GCA

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This study has been transitioned to CTIS with ID 2023-505476-29-00 check the CTIS register for the current data. This study consists of two periods. The objective of Period 1 is to evaluate the efficacy of upadacitinib in combination with a 26-week...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON52668

Source
ToetsingOnline

Brief title
M16-852

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Arteritis, Giant Cell Arteritis (GCA)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Adults, Giant Cell Arteritis (GCA), Upadacitinib

Outcome measures

Primary outcome

The proportion of subjects achieving sustained remission at Week 52 as defined

as:

-Absence of GCA signs and symptoms from Week 12 through Week 52

-Adherence to the protocol defined corticosteroid taper regimen

Secondary outcome

Key secondary endpoints include:

• Proportion of subjects achieving sustained complete remission from Week 12

through Week 52. Sustained complete remission is defined as having achieved all

of the following:

- Absence of GCA signs and symptoms from Week 12 through Week 52;

- Normalization of erythrocyte sedimentation rate ([ESR] to < 30 mm/hr without

elevation to >= 30 mm/hr [attributable to GCA]) from Week 12 through Week 52;

- Normalization of high sensitivity C-reactive protein ([hsCRP] to < 1 mg/dL

without elevation (on 2 consecutive visits) to >= 1 mg/dL from Week 12 through

Week 52; and

- Adherence to the protocol-defined CS taper regimen.

• Cumulative CS exposure.

• Time to first disease flare. Disease flare is defined as an event determined by the investigator to represent recurrence of GCA signs or symptoms or an ESR measurement >= 30 mm/hr (attributable to GCA), AND requiring an increase in CS dose.

• Proportion of subjects who experience at least 1 disease flare through Week 52.

• Proportion of subjects in complete remission at Week 52. Complete remission is defined as having achieved all of the following:

- Absence of GCA signs and symptoms;

- Normalization of ESR to < 30 mm/hr;

- Normalization of hsCRP to < 1 mg/dL; and

- Adherence to the protocol-defined CS taper regimen.

• Proportion of subjects in complete remission at Week 24.

• Change from Baseline in the 36-item Short Form Quality of Life Questionnaire (SF-36) Physical Component Score (PCS) at Week 52.

• Number of disease flares per subject during Period 1.

• Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) at Week 52.

• Assessment of Treatment Satisfaction Questionnaire for Medication (TSQM) patient global satisfaction subscale at Week 52.

• Rate of CS-related (AEs).

Study description

Background summary

Giant cell arteritis (GCA), also known as temporal arteritis, is a systemic vasculitis of the large vessels with a predilection for the cranial branches of the aorta. The course of GCA is characterized by a relatively abrupt onset followed by chronic vascular and systemic inflammation. Corticosteroid (CS) therapy is the current mainstay of treatment for GCA. Though many symptoms resolve rapidly with initiation of high dose CS therapy, there are cases reported of chronic underlying vascular inflammation and progression of vascular pathology despite control of clinically apparent disease activity. Thus, there remains the potential for improved treatment options which can mitigate this subclinical vascular inflammation.
Evidence suggests that inhibition of Janus kinase (JAK)-mediated pathways may be a promising approach for the treatment of subjects with GCA. More selective JAK inhibitors may decrease the risk for infection (including viral reactivation) and/or malignancy that are observed with pan JAK inhibitor or less selective JAK inhibitors. AbbVie is developing a small molecule inhibitor of JAK, upadacitinib,that may address the current needs for subjects with GCA.

Study objective

This study has been transitioned to CTIS with ID 2023-505476-29-00 check the CTIS register for the current data.

This study consists of two periods. The objective of Period 1 is to evaluate the efficacy of upadacitinib in combination with a 26-week corticosteroid (CS) taper regimen compared to placebo in combination with a 52-week CS taper regimen, as measured by the proportion of participants in sustained remission at Week 52, and to assess the safety and tolerability of upadacitinib in participants with giant cell arteritis (GCA).
The objective of period 2 is to evaluate the safety and efficacy of continuing versus withdrawing upadacitinib in maintaining remission in participants who achieved remission in Period 1.

Study design

To evaluate the Safety and Efficacy of Upadacitinib in Subjects with Giant Cell Arteritis. The study is comprised in 35-day maximum Screening Period: a 52 week randomized, double-blind, parallel-group treatment period (Period 1); a 52-week randomized, blinded extension period (Period 2); and a 30-day follow-up period.

Intervention

Experimental: Arm A
Upadacitinib dose A administered daily + 26-week CS taper regimen

Experimental: Arm B
Upadacitinib dose B administered daily + 26-week CS taper regimen
Placebo Comparator: Arm C
Placebo administered daily + 52-week CS taper regimen

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.
Subjects will either receive in period 1: upadacitinib + CS taper, or CS taper +placebo during the study. Subjects will receive upadacitinib or placebo during period 2 of 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. The majority of these patients did not have any muscle symptoms and did not stop study drug because of elevated CPK levels.
The hypothesis that upadacitinib will result in improved ability to maintain remission with absence of GCA signs and symptoms, 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 GCA. The subject*s condition may get better, may worsen, or may stay unchanged.

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

• Adult male or female, at least 50 years of age
• History of ESR >= 50 mm/hour of CRP >= 1.0 mg/dL
• Presence of unequivocal cranial symptoms of GCA or unequivocal symptoms of polymyalgia
rheumatica

Exclusion criteria

1. Prior exposure to any JAK inhibitor.
2. Treatment with an interleukin-6 (IL-6) inhibitor within 4 weeks of study start, or prior treatment
with an IL-6 inhibitor and experienced a disease flare during treatment
3. Subject must not have received a biologic or non-biologic DMARD within at least five times the
mean terminal elimination half-life of the drug.
4. Current or past history of infection including herpes zoster or herpes simplex, HIV, active
Tuberculosis, active or chronic recurring infection, active hepatitis B or C.
5. Female who is pregnant, breastfeeding, or considering pregnancy during the study

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:	Recruiting
Start date (anticipated):	20-02-2020
Enrollment:	16
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	13-03-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-05-2019
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-06-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-06-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-07-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-07-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-07-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-11-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-01-2020
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-05-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-07-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-11-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-12-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-01-2021
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Approved WMO Date:	13-03-2021
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Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-10-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-02-2023
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-12-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-03-2024
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
EU-CTR	CTIS2023-505476-29-00
EudraCT	EUCTR2017-003978-13-NL
CCMO	NL68201.042.19