A randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of sarilumab in patients with giant cell arteritis

Published: 09-10-2018
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Primary:To evaluate the efficacy of sarilumab in patients with giant cell arteritis (GCA) as assessed by the proportion of patients with sustained remission for sarilumab compared to placebo, in combination with a corticosteroid (CS) tapering course...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON45913

Source
ToetsingOnline

Brief title
EFC15068

Condition

- Autoimmune disorders

Synonym
Giant Cell Arteritis, Horton Disease, Temporal Arteritis

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis

Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Adults, Double-blind, Giant Cell Arteritis, Sarilumab

Outcome measures

Primary outcome

Proportion of patients achieving sustained remission at Week 52.

Secondary outcome

Summary of the components of the sustained remission composite measure at Week

52

Total cumulative corticosteroid (including prednisone) dose over 52 weeks.

Duration of first GCA flare from clinical remission up to Week 52.

Changes from baseline in the glucocorticoid toxicity index and its components

up to Week 52.

Number of adverse events.

Serum concentrations of sarilumab.

Study description

Background summary

Giant cell arteritis (also known as temporal arteritis; GCA) is an inflammation of the lining of the arteries that most often affects the arteries in the head, especially those in the temples. This disease can cause headaches, temporal tenderness, difficulties with vision and sometimes
permanent visual loss in one or both eyes. Patients may also experience feel morning stiffness, pain in your hip and/or shoulders, which may cause difficulty with raising arms or lifting legs. It is still not known yet what causes GCA, but it is known that the body*s immune system attacks and inflames the arteries though the reason is unknown.

The current standard of care for GCA is corticosteroid therapy. Although high dose CSs have generally been effective for the treatment of acute disease and control of inflammation, usually a year or more of coritcosteroid (CS) therapy is required for maintenance of
remission or control of disease activity. However, long term use of corticosteroids can cause severe side effects.

Interleukin-6 (IL-6) is a protein of the immune system which proves to play a significant rol in GCA. Recent studies demonstrate that blocking the IL-6 protein could be an adequate treatment for GCA.

Sarilumab, the study treatment, belongs to the group of monoclonal antibodies. It blocks the receptor of the IL-6 protein. It is registered wordwide for the treatment of rheumatoid arteritis.

Study objective

Primary:
To evaluate the efficacy of sarilumab in patients with giant cell arteritis (GCA) as assessed by the proportion of patients with sustained remission for sarilumab compared to placebo, in combination with a corticosteroid (CS) tapering course.

Secondary:
To demonstrate the efficacy of sarilumab in patients with GCA compared to placebo, in combination with CS taper with regards to:
-Clinical responses (such as responses based on disease remission rates, time to first disease flare) over time.
-Cumulative CS (including prednisone) exposure.
-To assess the safety (including immunogenicity) and tolerability of sarilumab in patients with GCA.
-To measure sarilumab serum concentrations in patients with GCA.
-To assess the effect of sarilumab on sparing glucocorticoid toxicity as measured by glucocorticoid
toxicity index (GTI).

Study design

Phase 3, randomized; double blind; 4 arms parallel.

Intervention

Sarilumab or placebo (subcutane).
Prednisone or placebo (oral).

Study burden and risks

Risks and burdens related to blood collection, study procedures and possible adverse events.

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

- Diagnose of Giant Cell Arteritis (GCA) according to European League Against Rheumatism/American College of Rheumatology classification criteria.
- New onset active disease or refractory active disease.
- At least one of the symptoms of GCA within 6 weeks of baseline.
- Either erythrocyte sedimentation rate * 30 mm/hour or C-reactive protein * 10 mg/L within 6

weeks of baseline.
- Receiving or able to receive prednisone 20-60 mg/day for the treatment of active GCA.

Exclusion criteria

- Organ transplantation recipient (except corneas, unless it is within 3 months prior to baseline visit).
- Major ischemic event, unrelated to GCA, within 12 weeks of screening.
- Prior treatment with any of the following:
> Janus kinase (JAK) inhibitor within 4 weeks of baseline.
> Cell-depletion agents without evidence of recovery of B cells to baseline level.
> Abatacept within 8 weeks of baseline.
> Anakinra within 1-week of baseline.
> Tumor necrosis factor (TNF) inhibitors within 2 to 8 weeks of, or less than at least 5 half-lives have elapsed prior to, baseline, whichever is longer.
- Therapeutic failure with biological Interleukin 6/(R) (IL-6/(R) antagonist.
- Alkylating agents including cyclophosphamide within 6 months of baseline.
- Use of immunosuppressants, such as hydroxychloroquine (HCQ), cyclosporine (CsA), azathioprine (AZA) or mycophenolate mofetil (MMF) or leflunomide (LEF) within 4 weeks of baseline. (Use of MTX not exceeding 25 mg per week and have been stable for at least 3 months prior to baseline is not exclusionary).
- Concurrent use of systemic CS for conditions other than GCA.
- Use of IV CS at a dose equivalent to 100 mg of methylprednisolone or higher within 8 weeks of baseline for GCA therapy.
- Pregnant or breastfeeding woman.
- Patients with active or untreated tuberculosis.
- Patients with history of invasive opportunistic infections.
- Patients with fever associated with infection or chronic, persistent or recurring infections requiring active treatment.
- Patients with uncontrolled diabetes mellitus.
- Patients with non-healed or healing skin ulcers.
- Patients who received any live, attenuated vaccine within 3 months of baseline.
- Patients who are positive for hepatitis B, hepatitis C and/or HIV.
- Patients with a history of active or recurrent herpes zoster.
- Patients with a history of or prior articular or prosthetic joint infection.
- Prior or current history of malignancy.
- Patients who have had surgery within 4 weeks of screening or planned surgery during the study.
- Patients with a history of inflammatory bowel disease or severe diverticulitis or previous gastrointestinal perforation.

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:	Recruitment stopped
Start date (anticipated):	25-07-2019
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kevzara
Generic name:	sarilumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Prednisone
Generic name:	Cortancyl
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	09-10-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	10-12-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	17-05-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	11-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	24-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	27-03-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	09-04-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	08-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	30-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
Other	2017-002988-18
EudraCT	EUCTR2017-002988-18-NL
CCMO	NL66747.058.18