ANIfrolumab treatment for 24 weeks in patients with primary Sjögren*s syndrome - Efficacy and safety assessment in a randomized, double-blind, placebo-controlled phase-IIa proof-of-concept trial (ANISE-II)

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This study has been transitioned to CTIS with ID 2024-516770-29-00 check the CTIS register for the current data. The objective of this study is to evaluate the clinical efficacy, biological effects and safety of anifrolumab treatment in pSS.

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

Summary

ID

NL-OMON51816

Source
ToetsingOnline

Brief title
ANISE-II

Condition

- Autoimmune disorders

Synonym
Primary Sjögren's syndrome

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Astra Zeneca,AstraZeneca BV

Intervention

Keyword: Anifrolumab, Primary Sjögren's syndrome, Randomised controlled trial

Outcome measures

Primary outcome

The selected primary outcome measure is the Composite of Relevant Endpoints for Sjögren*s Syndrome (CRESS) response at week 24. The CRESS is a recently developed composite endpoint which consists of five clinically relevant items for pSS: a systemic disease activity, patient-reported symptoms, tear gland, salivary gland and serology item. A CRESS responder is someone who reached response on at least three out of five items.

Secondary outcome

1. Safety (adverse events and tolerability) of anifrolumab by monitoring serious adverse events (SAE) and AE, treatment discontinuation related to SAE and AE, and lab abnormalities at weeks 0, 4, 8, 12, 16, 20 and 24.

2. Total CRESS response at week 12

3. Individual CRESS items (continuous): Clinical EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (weeks 0, 8, 12, 20, 24), EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) (weeks 0, 8, 12, 20, 24), Schirmer*s test (weeks 0, 12, 24), Ocular Staining Score (OSS) (weeks 0, 12, 24), unstimulated whole salivary flow (UWS) (weeks 0, 12, 24), Salivary gland

ultrasonography (SGUS) (Hocevar score) (weeks 0, 12, 24), rheumatoid factor (RF) and total IgG concentration in blood (weeks 0, 8, 12, 20, 24).

4. ESSDAI (continuous) (weeks 0, 8, 12, 20, 24)

5. The (Clin)ESSDAI minimal clinically important improvement (MCII, defined as decrease of >=3 points) and low disease activity (LDA, defined as score<5) (weeks 8, 12, 20, 24)

6. Physician global disease activity (GDA) (weeks 0, 8, 12, 20, 24)

7. NRS score oral, ocular, and vaginal dryness and mental fatigue (weeks 0, 8, 12, 20, 24)

8. Patient GDA (weeks 0, 8, 12, 20, 24)

9. Short form-36 (SF-36) health survey (weeks 0, 12, 24)

10. EuroQoL-5 dimensions (EQ-5D) measure of health-related quality of life (weeks 0, 8, 12, 20, 24)

11. Multidimensional Fatigue Index (MFI) scale (weeks 0, 12, 24)

12. Female Sexual Function Index (FSFI) in females (weeks 0, 12, 24)

13. Stimulated whole salivary flow (SWS) (weeks 0, 12, 24)

14. SGUS OMERACT score (weeks 0, 12, 24)

15. Parotid gland histology at baseline vs. week 24: focus score and area fraction of CD45+ infiltrate

16. Serum levels of anti-SSA/-SSB, complement (C3/C4), lymphocyte count, and presence of cryoglobulinemia (weeks 0, 8, 12, 20, 24)

Study description

Background summary

We aim to evaluate safety and determine the effects of anifrolumab on essential clinical and biological parameters in patients with primary Sjögren*s syndrome (pSS). Although the pathogenesis of pSS has not been fully elucidated, one of the key immune pathways involved is type-I IFN signalling. Since anifrolumab is a fully human, IgG1* monoclonal antibody to type-I interferon receptor subunit 1, we hypothesize that inhibition of type-I IFN signalling by anifrolumab may reduce glandular and systemic inflammation and attenuate disease activity in patients with pSS.

Study objective

This study has been transitioned to CTIS with ID 2024-516770-29-00 check the CTIS register for the current data.

The objective of this study is to evaluate the clinical efficacy, biological effects and safety of anifrolumab treatment in pSS.

Study design

This study is a randomized, double-blind, placebo-controlled phase IIa proof-of-mechanism trial. Thirty patients are randomized in a 2:1 ratio to either anifrolumab or placebo treatment, with which they will be treated for 24 weeks.

Intervention

Anifrolumab vs. placebo treatment. Anifrolumab 300 mg will be administered in intravenous infusions, once per 4 weeks, for a total treatment duration of 24 weeks. In total, participants will have 6 infusions during the study.

Study burden and risks

Primary SS has a major impact on patients* daily life. Apart from symptoms and extraglandular manifestations related to pSS, patients may also be restricted in their activities and their participation in society, resulting in a reduced HR-QoL and an impaired socioeconomic status. Consequently, there is a great need for developing adequate treatment modalities to reduce pSS-related complaints and to intervene in the progression of SS. Despite a number of recent, large RCTs with several promising (biological) drugs for pSS, no phase III trial was able to demonstrate beneficial treatment effects compared to placebo. This means that an unmet need for effective therapies in pSS remains and that there is a need to develop new treatment interventions. Both patients and physicians are willing to contribute to research to find effective therapies for pSS.

We realize that this study protocol is intensive with frequent visits to the outpatient clinic and consequently several tests, including parotid gland biopsies, and that certain risks (SAEs or AEs) are involved in this treatment. The most common side effects of anifrolumab according to the RCTs conducted in systemic lupus erythematosus (SLE) are upper respiratory tract infection, nasopharyngitis, infusion-related reaction, bronchitis and herpes zoster. However, an imbalance in adverse events between anifrolumab and placebo has not been observed in the previous trials. However, we assume, based on clinical experience and the available literature on anifrolumab in SLE and what we know of the underlying pathogenesis of pSS, that the advantages of participation in this trial outweigh the burden and risks involved with this treatment. Based on the rationale of this study and the experience with anifrolumab in SLE, we expect a positive effect of anifrolumab on pSS. Furthermore, patients may take advantage of close monitoring during this trial (e.g. information, support, early treatment of symptoms and extraglandular manifestations, early detection of possible MALT lymphomas).

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Written informed consent.
- Female or male aged >= 18 years.
- Disease duration <= 10 years.
- Fulfillment of the 2016 ACR/EULAR classification criteria for primary Sjögren's syndrome.
- ESSDAI >=5 and/or ESSPRI >=5. ESSDAI >=5 implicates a moderate to high systemic disease activity and ESSPRI >=5 implicates that the patient-reported symptom state is unacceptable. At least 50% of patients need to fulfil the ESSDAI >=5 criterion. Inclusion of patients with low ESSDAI (<5) should be discontinued when 50% have a low ESSDAI.
- Willingness to undergo a repeated biopsy. Baseline biopsy <=1 year before inclusion and follow-up biopsy 24 weeks after start treatment.
- Use of reliable method of contraception for participants of reproductive potential.
- Fully vaccinated against SARS-CoV-2, based on the current vaccine recommendations for immunocompromised patients.
- Weight of >= 40 kg.

Exclusion criteria

- Presence of any other connective tissue disease.
- Positive pregnancy test at screening or breastfeeding.
- History of alcohol or drug abuse.
- History of malignancy or with a current suspicion for cancer, apart from local MALT lymphoma, squamous or basal cell carcinoma of the skin treated with documented success of curative therapy <=3 months prior to week 0 or cervical cancer in situ treated with apparent success with curative therapy <=1 years prior to week 0.
- Subjects with evidence (as assessed by the investigator) of active or latent bacterial or viral infections at the time of potential enrollment, including subjects with evidence of HIV which will be tested during screening.
- History of chronic or recurrent serious infections.
- Subjects who have received any live or attenuated vaccines within 8 weeks prior to signing the ICF.
- Blood transfusion or receipt of blood products within 4 weeks prior to signing the ICF.
- Underlying cardiac, pulmonary, metabolic, renal, hepatic, gastrointestinal, hematological or neurological conditions, chronic or latent infectious diseases

or immune deficiency which places the patient at an unacceptable risk for participation in this study.
- Preceding treatment with biological DMARDs, including abatacept, anti-TNF or other monoclonal antibodies within 6 months, and rituximab within 12 months from baseline.
- Use of high-dose prednisone, less than 2 weeks before inclusion. Stable low dose (<= 10 mg) is allowed.
- Use of hydroxychloroquine, methotrexate, cyclophosphamide, cyclosporine, azathioprine, MMF and leflunomide less than 3 months ago.

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:	Recruiting
Start date (anticipated):	09-10-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Saphnelo
Generic name:	Anifrolumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-04-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-08-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-06-2024
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	CTIS2024-516770-29-00
EudraCT	EUCTR2022-000609-28-NL
CCMO	NL80976.042.22