A 48-week, 6-arm, randomized, double-blind, placebo-controlled multicenter trial to assess the safety and efficacy of multiple CFZ533 doses administered subcutaneously in two distinct populations of patients with Sjögren*s Syndrome (TWINSS)

Published: 13-06-2019
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The purpose of this trial is to- determine the dose-response of iscalimab in a population of patients with moderate-to-severe Sjögren*s Syndrome (SjS), defined by ESSDAI >=5and ESSPRI >=5 (Cohort 1)- evaluate the preliminary efficacy and...

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

Summary

ID

NL-OMON52778

Source
ToetsingOnline

Brief title
CCFZ533B2201 (TWINSS)

Condition

- Autoimmune disorders

Synonym
Sjogren syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: CFZ, Phase 2, Placebo, Sjogren

Outcome measures

Primary outcome

The primary objectives of the study are defined separately for each cohort.

Cohort 1:

To demonstrate a dose-response of CFZ533 (iscalimab) based on change in ESSDAI

from baseline at Week 24.

Cohort 2:

To estimate the effect of CFZ533 (iscalimab) 600 mg s.c. on the change in

ESSPRI at Week 24.

Secondary outcome

Cohort 1

To demonstrate a dose response of iscalimab based on change in ESSPRI from

baseline at Week 24

To estimate the effects of iscalimab based on

-change in FACIT-F from baseline at Week 24

- change in physician's global assessment (PhGA) from baseline at Week 24

To assess

the effect of iscalimab in the serum Free Light Chains (FLC) levels over time

the changes in IgG and IgM levels over time after iscalimab treatment

the effect of iscalimab on plasma CXCL-13 over time.

Cohort 2

To estimate the effects of iscalimab based on changes in

- FACIT-F from baseline at Week 24

- Physician's global assessments from baseline at Week 24

- ESSDAI from baseline at Week 24

To evaluate the efficacy of iscalimab in improving the dry eye

symptoms measured by IDEEL at Week 24

To assess

- the effect of iscalimab in the serum Free Light Chains (FLC) levels over time

- the changes in IgG and IgM levels over time after iscalimab

treatment

- the effect of iscalimab on plasma CXCL-13 over time.

Cohort 1 & 2

To assess

- safety and tolerability of iscalimab

- immunogenicity of iscalimab

- the pharmacokinetics and dose-exposure relationship of iscalimab

To measure soluble CD40 in plasma

Study description

Background summary

Sjögren*s Syndrome (SjS) is a chronic autoimmune disease of unknown etiology, characterized by lymphoid
infiltration and progressive destruction of exocrine glands. Current
standard-of-care (SoC) treatment for SjS patients is
limited to symptomatic care for the mucosal signs and symptoms (dryness).
Steroids and conventional disease
modifying antirheumatic drugs (DMARDs), although used in selected patients,
have not been proven efficacious, and
no pharmacologic intervention is effective against the severe, disabling
fatigue. Hence, there are no approved
treatments available for active, systemic disease.

The therapeutic hypothesis was successfully tested in a first proof-of-concept (PoC) study of
iscalimab in patients with primary Sjögren's Syndrome. Briefly, in this randomized controlled
trial, the primary endpoint of European Sjögren*s Syndrome Disease Activity Index (ESSDAI)
improvement was met, along with improvements in patient reported outcomes (PRO) including
fatigue. The overall risk/benefit profile was favorable, warranting continued development in this indication.

Study objective

The purpose of this trial is to
- determine the dose-response of iscalimab in a population of patients with moderate-to-severe Sjögren*s Syndrome (SjS), defined by ESSDAI >=5 and ESSPRI >=5 (Cohort 1)
- evaluate the preliminary efficacy and safety of iscalimab administered in a population of patients with low ESSDAI (<5) but high symptom burden (Cohort 2) defined by: ESSPRI fatigue >=5 or ESSPRI dryness >=5 and moderate ocular disease burden as measured by the Impact of Dry Eye on Everyday Life (IDEEL) questionnaire.

Study design

Study CFZ533B2201 (TWINSS) is a double-blind, randomized, placebocontrolled,

multicenter study to evaluate the safety, efficacy, PK and PD of multiple doses of CFZ533 in 2 distinct populations of patients with 1) moderate-to-severe SjS (systemic and symptomatic involvement) and 2) low systemic involvement but high symptom burden.

Intervention

CFZ533 or placebo

Study burden and risks

Minimum of 31 visits, duration vary from 1-4 hours per visit, total study time minimal 66 weeks.

Physical examination: Cohort 1: 15 times Cohort 2: 16 times
ECG: Cohort 1:one time, Cohort 2: One time
Schirmer test: Cohort 1: 6 times, Cohort 2: 6 times
Salivary flow rate (unstimulated) cohort 1: 5 times and cohort 2: 5 times
Stimulated Cohort 1: 9 times Cohort 2: 9 times
Salivary gland biopsy (optional): Cohort 1 and Cohort 2: 2 times
Questionnaires: Cohort1:25 times Cohort 2: 25 times
Patient diary: cohort 1: 27 times, cohort 2: 27 times
Arm- worn wearable device: To measure physical activity (optional): cohort 1 and 2: 8 times
Cognitive assessments: cohort 1: 4 times cohort 2: 4 times

Contacts

Public
Novartis

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Amsterdam 1101 BX
NL
Scientific
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

•Signed informed consent;
•Male or female patient >= 18 years of age;
•Classification of Sjögren's Syndrome according to ACR/EULAR 2016 criteria (Shiboski et al 2017);
•Seropositive for anti-Ro/SSA antibodies;
•Stimulated whole salivary flow rate of >= 0.1 mL/min;

Inclusion criteria specific for Cohort 1;
•ESSDAI >= 5 within the 8 predefined organ domains;
•ESSPRI score of >=5;

Inclusion criteria specific for Cohort 2;
•ESSDAI < 5 within 8 domains scored for inclusion criterion #7 Cohort 1;
•ESSPRI fatigue subscore >= 5 or ESSPRI dryness subscore >= 5;

Other protocol-defined inclusion criteria may apply.

Exclusion criteria

•Sjögren's Syndrome overlap syndromes where another autoimmune rheumatic disease constitutes the principle illness;
•Use of other investigational drugs;
•Use of B cell depleting therapies within 6 months prior to randomization, abatacept or any other immunosuppressants unless specifically allowed in the protocol;
•Use of steroids at dose > 10 mg/day;
•Uncontrolled ocular rosacea (affecting the eye adnexa), posterior blepharitis

or Meibomian gland disease (this criterion applies only to patients considered for Cohort 2);
•Active viral, bacterial or other infections requiring systemic treatment;
•Receipt of live/attenuated vaccine within a 2-month period prior to randomization, during treatment and for at least 14 weeks thereafter;
•Chronic infection with hepatitis B (HBV) or hepatitis C (HCV);
- Evidence of active CMV infection in the form of a positive serology for CMV IgM (in the absence or presence of positive CMV IgG) and/or quantifiable CMV DNA by PCR at screening.
•Evidence of active tuberculosis (TB) infection.

Other protocol-defined exclusion criteria may apply.

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:	Recruitment stopped
Start date (anticipated):	01-07-2020
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.

Generic name:	Iscalimab

Ethics review

Approved WMO Date:	13-06-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-03-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-10-2020
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-01-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	03-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2018-004476-35-NL
ClinicalTrials.gov	NCT03905525
CCMO	NL69847.078.19