A TWINSS extension trial to evaluate the safety and tolerability of CFZ533 (iscalimab) at two dose levels administered subcutaneously in patients with Sjögren*s Syndrome

Published: 10-05-2021
Last updated: 19-08-2024

The primary objective of this study is to evaluate the safety and tolerability of iscalimab at two dose levels (600 mg and 300 mg) in patients withSjögren*s Syndrome, who participated in the TWINSS core study,CCFZ533B2201.Secondary...

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

Summary

ID

NL-OMON51920

Source
ToetsingOnline

Brief title
CCFZ533B2201E1

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: CFZ533, iscalimab, Sjögren□s Syndrome, subcutaneous injection, TWINNS extension

Outcome measures

Primary outcome

- Incidence of Treatment-emergent adverse events (TEAEs)/ serious adverse

events (SAEs)

- Routine hematology and clinical chemistry laboratory test results at analysis

visits up to end of study

- Vital signs at analysis visits up to end of study

Secondary outcome

- Free iscalimab concentration in plasma during the treatment (Ctrough) and

follow-up (up to end of study) periods

- Incidence of anti-iscalimab antibodies in plasma at analysis visits up to end

of study

- The full list of exploratory endpoints to be included in the Clinical Study

Report (CSR) and corresponding analysis methods will be

detailed in the Statistical Analysis Plan (SAP)

- Biomarker levels during the treatment and follow-up (up to end of study)

periods

- Free or total soluble CD40 in the absence or presence of iscalimab,

respectively, at analysis visits up to end of study

-Biomarker levels during the treatment and follow-up (up to end of study)

periods

- Physical activity and vital sign parameters levels as measured with wearable

device during the treatment and follow-up (up to end of study) periods

Patient Health Questionnaire-2 (PHQ-2) total score and cognitive tests scores

as measured with smartphone application during the treatment and follow-up (up

to end of study) periods

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.

Limited safety data are currently available for iscalimab in any indication that is under investigation. This extension study (CCFZ533B2201E1) will allow us to demonstrate the additional safety and tolerability of two doses (600 mg and 300 mg) of treatment with iscalimab in patients with Sjögren's Syndrome (SjS).

Study objective

The primary objective of this study is to evaluate the safety and tolerability of iscalimab at two dose levels (600 mg and 300 mg) in patients with Sjögren*s Syndrome, who participated in the TWINSS core study,CCFZ533B2201.

Secondary Objectives
Objective 1: To assess the pharmacokinetics (PK trough levels) and dose exposure relationship of iscalimab
Objective 2: To assess immunogenicity of iscalimab

Study design

Study CCFZ533B2201E1 is a multicenter extension study. Study blinding for the extension study will be maintained until final database lock of the core study, CCFZ533B2201, upon which the participants and Investigators will be unblinded, making it an open-label study through Week 120 (end of study visit).

Intervention

CFZ533

Study burden and risks

Minimum of 28 visits, duration vary from 1-3 hours per visit, total study time 30 months.

Physical examination: 15 times
ECG: 1 time
Questionnaires: 7 times
Patient diary: completion every week
Arm- worn wearable device: To measure physical activity (optional): 7 times
Cognitive assessments: 7 times

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Participants must have participated in the TWINSS core study, CCFZ533B2201, and must have completed the entire treatment period up to Week 48 and the follow-up period up to Week 60
2. Signed informed consent must be obtained prior to participation in the extension study (i.e. before commencement of the Week 60 assessments of the core study)
3. In the judgement of the Investigator, participants must be expected to clinically benefit from continued iscalimab therapy

Exclusion criteria

1. Sjögren's Syndrome overlap syndromes where another autoimmune rheumatic disease constitutes the principle illness, specifically:
Moderate-to-severe active systemic lupus erythematosus (SLE) with anti-dsDNA positivity and renal involvement, or other organ involvement that impedes on ability to score ESSDAI domains
- Active rheumatoid arthritis (RA) that impedes on the ability to score the ESSDAI articular domain
- Systemic sclerosis
- Any other concurrent connective tissue disease (e.g., lupus nephritis (LN), large vessel vasculitis (LVV), Sharp syndrome (mixed connective tissue disease) that is active and requires immunosuppressive treatment outside the scope of this trial and would impede on Sjögren's Syndrome organ domain assessments

2. Use of other investigational drugs other than iscalimab during the core study
3. Active uncontrolled viral, bacterial or other infections requiring systemic treatment at the time of enrollment, or history of recurrent clinically significant infection or of bacterial infections with encapsulated organisms

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-11-2021
Enrollment:	8
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	10-05-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	28-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-10-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-01-2022
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:	01-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-10-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-08-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-05-2024
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	EUCTR2020-001942-20-NL

Register	ID
ClinicalTrials.gov	NCT04541589
CCMO	NL77019.078.21