Clinical trial results:
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

Summary

EudraCT number	2020-001942-20
Trial protocol	HU GR DE PT FR NL IT SE
Global end of trial date	19 August 2024

Results information

Result version number	v1 (current)
This version publication date	28 June 2025
First version publication date	28 June 2025

Trial information

Trial identification

Sponsor protocol code	CCFZ533B2201E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04541589
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus,, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 January 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Chile: 21
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	Russian Federation: 30

Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Türkiye: 3
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	206
EEA total number of subjects	77

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	171
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who completed the core study (CCFZ533B2201, NCT03905525) and were deemed by the Investigator to clinically benefit from continued iscalimab therapy based upon response to therapy at the end of the treatment period of the core study were enrolled in this study

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

The study was conducted as a double-blind treatment until the final database lock of the Core study (NCT03905525). During this period, participants, Investigator, site staff, and persons performing the assessments remained blinded to the identity of the treatment until the final database lock of the core study

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1: Iscalimab 600 mg

Arm description:

Participants received 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously weekly for the initial 3 weeks as loading doses, followed by a bi-weekly maintenance regimen at 600 mg (2 injections of 300 mg/2 mL).

Arm type	Experimental
Investigational medicinal product name	Iscalimab
Investigational medicinal product code	CFZ533
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Iscalimab 600 mg or 300 mg was administered subcutaneously weekly for the first 3 weeks. Subsequently, iscalimab was administered subcutaneously bi-weekly (every other week or Q2W).

Arm title	Arm 2 - Iscalimab 300 mg

Arm description:

Participants received one dose of 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously on the first day of the extension study; then 300 mg weekly (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo) for the next 2 weeks as loading doses. This was followed by a bi-weekly maintenance regimen of 300 mg (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo). After the final database lock of the core study, participants underwent unblinding, leading to the discontinuation of placebo injections.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo (1 injection of 2 ml) administered to participants in the iscalimab 300 mg arm to mantain

blinding until the final database lock of the core study

Investigational medicinal product name	Iscalimab
Investigational medicinal product code	CFZ533
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Iscalimab 600 mg or 300 mg was administered subcutaneously weekly for the first 3 weeks. Subsequently, iscalimab was administered subcutaneously bi-weekly (every other week or Q2W).

Number of subjects in period 1	Arm 1: Iscalimab 600 mg	Arm 2 - Iscalimab 300 mg
Started	152	54
Completed	133	47
Not completed	19	7
Physician decision	3	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	8	2
Subject decision	7	4

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1: Iscalimab 600 mg
Reporting group description:	
Participants received 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously weekly for the initial 3 weeks as loading doses, followed by a bi-weekly maintenance regimen at 600 mg (2 injections of 300 mg/2 mL).	
Reporting group title	Arm 2 - Iscalimab 300 mg
Reporting group description:	
Participants received one dose of 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously on the first day of the extension study; then 300 mg weekly (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo) for the next 2 weeks as loading doses. This was followed by a bi-weekly maintenance regimen of 300 mg (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo). After the final database lock of the core study, participants underwent unblinding, leading to the discontinuation of placebo injections.	

Reporting group values	Arm 1: Iscalimab 600 mg	Arm 2 - Iscalimab 300 mg	Total
Number of subjects	152	54	206
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	126	45	171
>=65 years	26	9	35
Sex: Female, Male Units: Participants			
Female	148	53	201
Male	4	1	5
Race/Ethnicity, Customized Units: Subjects			
White	125	45	170
Black or African American	5	2	7
Asian	16	6	22
American Indian or Alaska Native	4	1	5
Unknown	2	0	2

End points

End points reporting groups

Reporting group title	Arm 1: Iscalimab 600 mg

Reporting group description:

Participants received 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously weekly for the initial 3 weeks as loading doses, followed by a bi-weekly maintenance regimen at 600 mg (2 injections of 300 mg/2 mL).

Reporting group title	Arm 2 - Iscalimab 300 mg

Reporting group description:

Participants received one dose of 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously on the first day of the extension study; then 300 mg weekly (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo) for the next 2 weeks as loading doses. This was followed by a bi-weekly maintenance regimen of 300 mg (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo). After the final database lock of the core study, participants underwent unblinding, leading to the discontinuation of placebo injections.

Primary: Number of participants with Treatment-emergent adverse events (TEAEs)

End point title	Number of participants with Treatment-emergent adverse events (TEAEs)[1]

End point description:

An AE was defined as any untoward medical occurrence (e.g., any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a participant. TEAE included all AEs up to the last dose date plus 14 weeks or the end of the entire study (including the safety follow-up period), whichever occurred earlier. A patient with multiple severity ratings for an AE was only counted under the maximum rating. Additionally, a patient with multiple occurrences of an event was counted only once. The severity of AEs was assessed using the Common Terminology Criteria for Adverse Events, with the following grading system: Mild: usually transient in nature and generally not interfering with normal activities; Moderate: sufficiently discomforting to interfere with normal activities; Severe: prevented normal activities.
A serious adverse event (SAE) was defined as any AE that required medical intervention, hospitalization, or results in death, disability, or a birth defect.

End point type	Primary

End point timeframe:

From start of extension study up to 14 weeks after last study-drug administration or end of study (whichever occurred earlier), assessed up to approximately 60 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this primary end point.

End point values	Arm 1: Iscalimab 600 mg	Arm 2 - Iscalimab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	54		
Units: Participants				
Death	0	0		
AE (all severities)	127	43		
AE- Mild	57	24		
AEt- Moderate	62	17		
AE- Severe	8	2		
SAE	13	2		
AE leading to treatment discontinuation	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Free iscalimab concentration in plasma

End point title	Free iscalimab concentration in plasma

End point description:

Free iscalimab concentration in plasma during the treatment (Ctrough) and follow-up (up to end of study) periods. Blood sample was collected at the specified timepoints to assess the concentration of free iscalimab. The baseline assessment of this extension study (Day 1) was identical to the last timepoint (FUP3/Week 60) of the core study (CCFZ533B2201).

End point type	Secondary

End point timeframe:

Predose at Day 1, 113, 225, 337 and 421

End point values	Arm 1: Iscalimab 600 mg	Arm 2 - Iscalimab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	52		
Units: microgram / mililiter				
geometric mean (geometric coefficient of variation)				
Day 1	3.56 (± 372.2)	451.8 (± 0.751)		
Day 113	125 (± 62.7)	56.9 (± 54.0)		
Day 225	126 (± 104.7)	50.3 (± 57.0)		
Day 337	138 (± 69.3)	62.6 (± 63.3)		
Day 421	4.47 (± 533.7)	350.4 (± 0.336)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-iscalimab antibodies in plasma

End point title	Incidence of anti-iscalimab antibodies in plasma

End point description:

Number of participants with anti-iscalimab antibodies (ADA) in plasma at any time during the study. The baseline assessment of this extension study (Day 1) was identical to the last timepoint (FUP3/Week 60) of the core study (CCFZ533B2201).

End point type	Secondary

End point timeframe:
60 weeks

End point values	Arm 1: Iscalimab 600 mg	Arm 2 - Iscalimab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	54		
Units: Participants	1	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of extension study up to 14 weeks after last study-drug administration or end of study (whichever occurred earlier), assessed up to approximately 60 weeks

Adverse event reporting additional description:

Any sign or symptom that occurred during the conduct of the trial and safety follow-up. The safety analyses were done on the safety population, which included all randomized subjects who received at least one dose of study medication. Patients were analyzed according to the actual treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Arm 2 - Iscalimab 300 mg

Reporting group description:

Participants received one dose of 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously on the first day of the extension study; then 300 mg weekly (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo) for the next 2 weeks as loading doses. This was followed by a bi-weekly maintenance regimen of 300 mg (1 injection of 300 mg/2 mL of iscalimab and 1 injection of 2 mL of placebo). After the final database lock of the core study, participants underwent unblinding, leading to the discontinuation of placebo injections.

Reporting group title	Arm 1: Iscalimab 600 mg

Reporting group description:

Participants received 600 mg (2 injections of 300 mg/2 mL) of iscalimab subcutaneously weekly for the initial 3 weeks as loading doses, followed by a bi-weekly maintenance regimen at 600 mg (2 injections of 300 mg/2 mL).

Serious adverse events	Arm 2 - Iscalimab 300 mg	Arm 1: Iscalimab 600 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 54 (3.70%)	13 / 152 (8.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 54 (1.85%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Status epilepticus			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 54 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulocytopenia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal prolapse			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			

subjects affected / exposed	1 / 54 (1.85%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Sjogren's syndrome			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bartholinitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	0 / 54 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm 2 - Iscalimab 300 mg	Arm 1: Iscalimab 600 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 54 (70.37%)	102 / 152 (67.11%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 54 (5.56%)	9 / 152 (5.92%)	
occurrences (all)	3	13	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 54 (3.70%)	10 / 152 (6.58%)	
occurrences (all)	3	16	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 54 (3.70%)	8 / 152 (5.26%)	
occurrences (all)	4	13	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 54 (7.41%)	13 / 152 (8.55%)	
occurrences (all)	4	16	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 54 (7.41%)	9 / 152 (5.92%)	
occurrences (all)	5	11	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 54 (9.26%)	9 / 152 (5.92%)	
occurrences (all)	7	13	
Back pain			

subjects affected / exposed	3 / 54 (5.56%)	5 / 152 (3.29%)	
occurrences (all)	3	6	
Osteoarthritis			
subjects affected / exposed	3 / 54 (5.56%)	7 / 152 (4.61%)	
occurrences (all)	3	7	
Infections and infestations			
Influenza			
subjects affected / exposed	7 / 54 (12.96%)	7 / 152 (4.61%)	
occurrences (all)	7	9	
Nasopharyngitis			
subjects affected / exposed	9 / 54 (16.67%)	22 / 152 (14.47%)	
occurrences (all)	17	32	
Oral herpes			
subjects affected / exposed	3 / 54 (5.56%)	7 / 152 (4.61%)	
occurrences (all)	6	13	
COVID-19			
subjects affected / exposed	16 / 54 (29.63%)	39 / 152 (25.66%)	
occurrences (all)	22	46	
Sinusitis			
subjects affected / exposed	3 / 54 (5.56%)	7 / 152 (4.61%)	
occurrences (all)	5	8	
Upper respiratory tract infection			
subjects affected / exposed	5 / 54 (9.26%)	19 / 152 (12.50%)	
occurrences (all)	5	26	
Urinary tract infection			
subjects affected / exposed	5 / 54 (9.26%)	16 / 152 (10.53%)	
occurrences (all)	6	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2021	The main purpose of the amendment was to include an additional assessment time point as part of the IRT algorithm criteria for participant rollover from the TWINSS core study (CCFZ533B2201) to extension study. ESSDAI and ESSPRI scores at Week 0 might be used for the IRT algorithm in the absence of a score at Week 4 of the core study. Specific guidance concerning public health emergency situations as declared by local or regional authorities (i.e., pandemic, epidemic or natural disaster) was also included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported