



Clinical trial results:

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 Sjogren's Syndrome (TWINSS)

Summary

EudraCT number	2018-004476-35
Trial protocol	PT HU GB NL GR FR DE SE AT SI IT RO
Global end of trial date	06 June 2023

Results information

Result version number	v1 (current)
This version publication date	20 June 2024
First version publication date	20 June 2024

Trial information

Trial identification

Sponsor protocol code	CCFZ533B2201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03905525
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	06 June 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives were to demonstrate for Cohort 1 a dose-response of CFZ533 (iscalimab) based on change in ESSDAI from baseline at Week 24, and to estimate for Cohort 2 the effect of CFZ533 (iscalimab) 600 mg subcutaneous (s.c.) on the change in ESSPRI at Week 24.

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	01 October 2019
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: 8
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Brazil: 14
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Chile: 26
Country: Number of subjects enrolled	Colombia: 9
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 16
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Portugal: 12
Country: Number of subjects enrolled	Romania: 7

Country: Number of subjects enrolled	Russian Federation: 34
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	United States: 22
Worldwide total number of subjects	273
EEA total number of subjects	100

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)	236
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted at 71 sites in 23 countries worldwide.

Period 1

Period 1 title	Period 1 (up to Week 24): Cohorts 1&2
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	Cohort 1 / Arm D (Period 1): Placebo
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Arm description:

Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.

Arm title	Cohort 1/Arm C: CFZ533 150 mg
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Arm description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm type	Experimental
Investigational medicinal product name	CFZ533 150 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm title	Cohort 1/Arm B: CFZ533 300 mg
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Arm description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm type	Experimental
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Investigational medicinal product name	CFZ533 300 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm title	Cohort 1/Arm A: CFZ533 600 mg
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Arm description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm type	Experimental
Investigational medicinal product name	CFZ533 600 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm title	Cohort 2/Arm F: Placebo
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Arm description:

Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.

Arm title	Cohort 2/Arm E: CFZ533 600 mg
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Arm description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm type	Experimental
Investigational medicinal product name	CFZ533 600 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25

Number of subjects in period 1	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg
Started	43	44	43
Full analysis set (FAS)	43	44	43
Continued to Treatment Period 2	41	42	41
Completed	41	42	41
Not completed	2	2	2
Physician decision	-	1	-
Adverse event, non-fatal	1	1	2
Subject decision	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Cohort 1/Arm A: CFZ533 600 mg	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg
Started	43	50	50
Full analysis set (FAS)	43	50	50
Continued to Treatment Period 2	39	45	48
Completed	39	44	48
Not completed	4	6	2
Physician decision	-	-	-
Adverse event, non-fatal	4	3	1
Subject decision	-	3	1
Lost to follow-up	-	-	-

Period 2

Period 2 title	Period 2 (up to Week 48): Cohorts 1&2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Cohort 1/Arm C: CFZ533 150 mg
Arm description:	
3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Arm type	Experimental

Investigational medicinal product name	CFZ533 150 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Arm title	Cohort 1/Arm B: CFZ533 300 mg
Arm description:	
3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Arm type	Experimental
Investigational medicinal product name	CFZ533 300 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Arm title	Cohort 1/Arm A: CFZ533 600 mg
Arm description:	
3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Arm type	Experimental
Investigational medicinal product name	CFZ533 600 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Arm title	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24)
Arm description:	
3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	
Arm type	Experimental
Investigational medicinal product name	CFZ 533 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Period 2: 3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	
Arm title	Cohort 2/Arm E: CFZ533 600 mg

Arm description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Arm type	Experimental
Investigational medicinal product name	CFZ533 600 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25

Arm title	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg
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Arm description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.

Arm type	Experimental
Investigational medicinal product name	CFZ533 300 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Period 2: 3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.

Number of subjects in period 2	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Started	42	41	39
Continued to Post-Tx FUP Period	42	40	39
Completed	38	36	39
Not completed	4	5	0
Adverse event, serious fatal	-	1	-
Withdrawal of Consent	-	1	-
Physician decision	-	1	-
Adverse event, non-fatal	1	1	-
Subject decision	3	1	-
Protocol deviation	-	-	-

Number of subjects in period 2	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24)	Cohort 2/Arm E: CFZ533 600 mg	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg
Started	41	48	45
Continued to Post-Tx FUP Period	41	46	45
Completed	39	41	44
Not completed	2	7	1

Adverse event, serious fatal	-	1	-
Withdrawal of Consent	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	1	1
Subject decision	2	4	-
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 / Arm D (Period 1): Placebo
Reporting group description: Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	
Reporting group title	Cohort 1/Arm C: CFZ533 150 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm B: CFZ533 300 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm A: CFZ533 600 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 2/Arm F: Placebo
Reporting group description: Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	
Reporting group title	Cohort 2/Arm E: CFZ533 600 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	

Reporting group values	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg
Number of subjects	43	44	43
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	38	38	39
From 65-84 years	5	6	4
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	53.3	49.3	48.7
standard deviation	± 9.55	± 14.41	± 12.78

Sex: Female, Male			
Units: Participants			
Female	41	42	41
Male	2	2	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	3	4	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	38	37	35
More than one race	1	1	1
Unknown or Not Reported	0	0	0

Reporting group values	Cohort 1/Arm A: CFZ533 600 mg	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg
Number of subjects	43	50	50
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	37	44	40
From 65-84 years	6	6	10
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	52.6	49.4	53.6
standard deviation	± 12.31	± 13.40	± 13.18
Sex: Female, Male			
Units: Participants			
Female	40	48	50
Male	3	2	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	5	7	8
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	3	3
White	35	38	37
More than one race	1	1	0
Unknown or Not Reported	0	1	1

Reporting group values	Total		
Number of subjects	273		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	236		
From 65-84 years	37		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	262		
Male	11		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4		
Asian	31		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	11		
White	220		
More than one race	5		
Unknown or Not Reported	2		

End points

End points reporting groups

Reporting group title	Cohort 1 / Arm D (Period 1): Placebo
Reporting group description: Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	
Reporting group title	Cohort 1/Arm C: CFZ533 150 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm B: CFZ533 300 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm A: CFZ533 600 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 2/Arm F: Placebo
Reporting group description: Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	
Reporting group title	Cohort 2/Arm E: CFZ533 600 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm C: CFZ533 150 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm B: CFZ533 300 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1/Arm A: CFZ533 600 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24)
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	
Reporting group title	Cohort 2/Arm E: CFZ533 600 mg
Reporting group description: 3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	
Reporting group title	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg

Reporting group description:

3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.

Subject analysis set title	Cohort 1: Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: Placebo	
Subject analysis set title	Cohort 1: CFZ533 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: CFZ533 150 mg	
Subject analysis set title	Cohort 1: CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: CFZ533 600 mg	
Subject analysis set title	Cohort 1: CFZ533 600 mg 24 Weeks
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: CFZ533 600 mg 24 Weeks	
Subject analysis set title	Cohort 1: CFZ533 150 mg 48 Weeks
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: CFZ533 150 mg 48 Weeks	
Subject analysis set title	Cohort 1: CFZ533 300 mg 48 Weeks
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: CFZ533 300 mg 48 Weeks	
Subject analysis set title	Cohort 1: CFZ533 600 mg 48 Weeks
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 1: CFZ533 600 mg 48 Weeks	
Subject analysis set title	Any CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All participants from cohort 1 who received CFZ533 600 mg in all Study Periods (including placebo patients who switched to CFZ533 600 mg at Week 24)	
Subject analysis set title	Any CFZ533
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All participants from cohort 1 who received a dose of CFZ533 during the study	
Subject analysis set title	Cohort 2: Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 2: Placebo	
Subject analysis set title	Cohort 2: CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 2: CFZ533 600 mg	
Subject analysis set title	Cohort 2: CFZ533 300 mg 24 Weeks
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Cohort 2: CFZ533 300 mg 24 Weeks	

Subject analysis set title	Cohort 2: CFZ533 600 mg 48 Weeks
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 2: CFZ533 600 mg 48 Weeks	
Subject analysis set title	Any CFZ533
Subject analysis set type	Sub-group analysis
Subject analysis set description: All participants from cohort 2 who received a dose of CFZ533 during the study	
Subject analysis set title	Cohort 1: Placebo - CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: Placebo - CFZ533 600 mg	
Subject analysis set title	Cohort 1: CFZ533 150 mg - CFZ533 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 150 mg - CFZ533 150 mg	
Subject analysis set title	Cohort 1: CFZ533 300 mg - CFZ533 300 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 300 mg - CFZ533 300 mg	
Subject analysis set title	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 600 mg - CFZ533 600 mg	
Subject analysis set title	Cohort 2: Placebo - CFZ533 300 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 2: Placebo - CFZ533 300 mg	
Subject analysis set title	Cohort 2: CFZ533 600 mg - CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 2: CFZ533 600 mg - CFZ533 600 mg	
Subject analysis set title	Cohort 1: Placebo - CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: Placebo - CFZ533 600 mg	
Subject analysis set title	Cohort 1: CFZ533 150 mg - CFZ533 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 150 mg - CFZ533 150 mg	
Subject analysis set title	Cohort 1: CFZ533 300 mg - CFZ533 300 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 300 mg - CFZ533 300 mg	
Subject analysis set title	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 600 mg - CFZ533 600 mg	
Subject analysis set title	Cohort 2: Placebo - CFZ533 300 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 2: Placebo - CFZ533 300 mg	

Subject analysis set title	Cohort 1: CFZ533 150 mg - CFZ533 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 150 mg - CFZ533 150 mg	
Subject analysis set title	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: CFZ533 600 mg - CFZ533 600 mg	
Subject analysis set title	Cohort 2: Placebo - CFZ533 300 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 2: Placebo - CFZ533 300 mg	

Primary: Cohort 1: Change in EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) score from baseline at 24 weeks as compared to placebo

End point title	Cohort 1: Change in EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) score from baseline at 24 weeks as compared to placebo ^[1]
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End point description:

ESSDAI is a validated disease outcome measure for SjS that contains 12 organ-specific domains contributing to disease activity. For each domain, features of disease activity are scored in 3 or 4 levels according to their severity. These scores are then summed across the 12 domains in a weighted manner to provide the total score. The domains (weights) are as follows: constitutional (3), lymphadenopathy (4), glandular (2), articular (2), cutaneous (3), pulmonary (5), renal (5), muscular (6), peripheral nervous system (PNS) (5), central nervous system (CNS) (5), hematological (2) and biological (1). The total score may vary between 0-123. It is considered low activity an ESSDAI < 5; moderate activity 5-13, and high activity if ESSDAI is ≥ 14.

End point type	Primary
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End point timeframe:

Baseline, Week 24

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 1

End point values	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	42	41	39
Units: Unit on a scale				
least squares mean (standard error)	-4.0 (± 0.73)	-7.0 (± 0.70)	-5.4 (± 0.71)	-6.9 (± 0.73)

Statistical analyses

Statistical analysis title	ESSDAI score at 24 weeks - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm C: CFZ533 150 mg

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0025
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	-1.1

Statistical analysis title	ESSDAI score at 24 weeks - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm B: CFZ533 300 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1578
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	0.5

Statistical analysis title	ESSDAI score at 24 weeks - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm A: CFZ533 600 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0037
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	-1

Primary: Cohort 2: Change in EULAR Sjögren Syndrome Patient Reported Index (ESSPRI) score from baseline at 24 weeks as compared to placebo.

End point title	Cohort 2: Change in EULAR Sjögren Syndrome Patient Reported Index (ESSPRI) score from baseline at 24 weeks as compared to placebo. ^[2]
End point description: The ESSPRI is a self-evaluation index for measuring symptoms including pain, fatigue and dryness. Each symptom was measured with a single 0 (no symptoms) to 10 (severe symptoms) numerical scale and the final ESSPRI score is calculated by averaging these domains with a maximum severity score of 10.	
End point type	Primary
End point timeframe: Baseline, Week 24	
Notes: [2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable to participants in Cohort 2	

End point values	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	49		
Units: Unit on a scale				
least squares mean (standard error)	-1.21 (± 0.271)	-1.79 (± 0.258)		

Statistical analyses

Statistical analysis title	ESSPRI score at 24 weeks - Cohort 2
Comparison groups	Cohort 2/Arm F: Placebo v Cohort 2/Arm E: CFZ533 600 mg
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.121
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.15

Secondary: Cohort 1: Change from baseline in ESSPRI at Week 24

End point title	Cohort 1: Change from baseline in ESSPRI at Week 24 ^[3]
End point description: The ESSPRI is a self-evaluation index for measuring symptoms including pain, fatigue and dryness. Each symptom was measured with a single 0 (no symptoms) to 10 (severe symptoms) numerical scale and the final ESSPRI score is calculated by averaging these domains with a maximum severity score of 10.	
End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 1

End point values	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	40	39
Units: Unit on a scale				
least squares mean (standard error)	-1.3 (\pm 0.31)	-1.8 (\pm 0.30)	-1.6 (\pm 0.31)	-1.8 (\pm 0.31)

Statistical analyses

Statistical analysis title	ESSPRI at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm C: CFZ533 150 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2078
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.3

Statistical analysis title	ESSPRI at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm A: CFZ533 600 mg
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1998
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-0.5
Confidence interval	
level	Other: 0.2 %
sides	2-sided
lower limit	-1.4
upper limit	0.3

Statistical analysis title	ESSPRI at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm B: CFZ533 300 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5132
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.6

Secondary: Cohort 1: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24

End point title	Cohort 1: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24 ^[4]
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End point description:

The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F version 4) is a 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue was measured on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much) except 2 items which were reversed scored. Final score range is 0-52 with lower scores indicating severe fatigue.

End point type	Secondary
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End point timeframe:

Baseline, 24 weeks

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 1

End point values	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	42	40	39
Units: Unit on a scale				
least squares mean (standard error)	7.0 (± 1.48)	8.6 (± 1.45)	8.0 (± 1.47)	10.3 (± 1.50)

Statistical analyses

Statistical analysis title	FACIT-F at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm C: CFZ533 150 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4363
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	5.6

Statistical analysis title	FACIT-F at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm A: CFZ533 600 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.105
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	7.3

Statistical analysis title	FACIT-F at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm B: CFZ533 300 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6181
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	5

Secondary: Cohort 1: Change from baseline in Physician Global Assessment (PhGA) at Week 24

End point title	Cohort 1: Change from baseline in Physician Global Assessment (PhGA) at Week 24 ^[5]
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End point description:

Physician's global assessment (PhGA) of disease activity was performed using a Visual Analog Scale (VAS) - an unnumbered 100 mm horizontal line ranging from "no disease activity" (score 0) to "maximal disease activity" (score 100). The assessment of patient's condition on the day is made by placing a vertical mark across the line.

End point type	Secondary
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End point timeframe:

Baseline, 24 weeks

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable to participants in Cohort 1

End point values	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	40	35	39
Units: Unit on a scale				
least squares mean (standard error)	-23.9 (± 2.94)	-31.6 (± 2.83)	-30.8 (± 3.00)	-27.0 (± 2.87)

Statistical analyses

Statistical analysis title	PhGA at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm C: CFZ533 150 mg
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0561
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.6
upper limit	0.2

Statistical analysis title	PhGA at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm B: CFZ533 300 mg

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0974
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	1.3

Statistical analysis title	PhGA at Week 24 - Cohort 1
Comparison groups	Cohort 1 / Arm D (Period 1): Placebo v Cohort 1/Arm A: CFZ533 600 mg
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4433
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	4.8

Secondary: Cohort 2: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24

End point title	Cohort 2: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24 ^[6]
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End point description:

The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F version 4) is a 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue was measured on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much) except 2 items which were reversed scored. Final score range is 0-52 with lower scores indicating severe fatigue.

End point type	Secondary
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End point timeframe:

Baseline, 24 weeks

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 2

End point values	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	49		
Units: Unit on a scale				
least squares mean (standard error)	5.7 (\pm 1.32)	7.3 (\pm 1.25)		

Statistical analyses

Statistical analysis title	FACIT-F at Week 24 - Cohort 2
Comparison groups	Cohort 2/Arm F: Placebo v Cohort 2/Arm E: CFZ533 600 mg
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3675
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	5.1

Secondary: Cohort 2: Change from baseline in Physician Global Assessment (PhGA) at Week 24

End point title	Cohort 2: Change from baseline in Physician Global Assessment (PhGA) at Week 24 ^[7]
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End point description:

Physician's global assessment (PhGA) of disease activity was performed using a Visual Analog Scale (VAS) - an unnumbered 100 mm horizontal line ranging from "no disease activity" (score 0) to "maximal disease activity" (score 100). The assessment of patient's condition on the day is made by placing a vertical mark across the line.

End point type	Secondary
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End point timeframe:

Baseline, 24 weeks

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 2

End point values	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	46		
Units: Unit on a scale				
least squares mean (standard error)	-10.4 (\pm 2.37)	-15.8 (\pm 2.29)		

Statistical analyses

Statistical analysis title	PhGA at Week 24 - Cohort 2
Comparison groups	Cohort 2/Arm F: Placebo v Cohort 2/Arm E: CFZ533 600 mg
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1014
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	1.1

Secondary: Cohort 2: Change from baseline in ESSDAI at Week 24

End point title	Cohort 2: Change from baseline in ESSDAI at Week 24 ^[8]
End point description: ESSDAI is a validated disease outcome measure for SjS that contains 12 organ-specific domains contributing to disease activity. For each domain, features of disease activity are scored in 3 or 4 levels according to their severity. These scores are then summed across the 12 domains in a weighted manner to provide the total score. The domains (weights) are as follows: constitutional (3), lymphadenopathy (4), glandular (2), articular (2), cutaneous (3), pulmonary (5), renal (5), muscular (6), peripheral nervous system (PNS) (5), central nervous system (CNS) (5), hematological (2) and biological (1). The final score may vary between 0-123. It is considered low activity an ESSDAI < 5; moderate activity 5-13, and high activity if ESSDAI is >= 14.	
End point type	Secondary
End point timeframe: Baseline, week 24	

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 2

End point values	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Unit on a scale				
least squares mean (standard error)	0.2 (± 0.33)	-0.3 (± 0.32)		

Statistical analyses

Statistical analysis title	ESSDAI at Week 24 - Cohort 2
Comparison groups	Cohort 2/Arm F: Placebo v Cohort 2/Arm E: CFZ533 600 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2694
Method	Mixed models analysis
Parameter estimate	LS Mean difference CFZ533-Placebo
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.4

Secondary: Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24

End point title	Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24 ^[9]
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End point description:

The distribution of adverse events in Treatment Period 1 was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters.

Analyses of data in the Safety Set (SAF) up to Week 24 (Period 1) is presented by actual treatment during Period 1, with data from separate cohort for the CFZ533 600mg and for the Placebo groups: CFZ533 600 mg, CFZ533 300 mg, CFZ533 150 mg and placebo.

End point type	Secondary
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End point timeframe:

Up to Week 24

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 1

End point values	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1: Placebo	Cohort 1: CFZ533 150 mg	Cohort 1: CFZ533 600 mg
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	43	44	44
Units: Participants				
Death	0	0	0	0
Adverse Event	32	31	38	35
Serious Adverse Event	3	1	1	4

AE leading to study medication discontinuation	1	1	1	5
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Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Proportion of subjects with at least 12 points improvement measured by score of Impact of Dry Eye on Everyday Life (IDEEL) questionnaire symptom bother module at Week 24.

End point title	Cohort 2: Proportion of subjects with at least 12 points improvement measured by score of Impact of Dry Eye on Everyday Life (IDEEL) questionnaire symptom bother module at Week 24. ^[10]
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End point description:

The Impact of Dry Eye on Everyday Life (IDEEL) questionnaire is a comprehensive dry eye specific questionnaire to evaluate treatment satisfaction, symptom-related bother and impact on daily life in a population with dry eye. This study only utilized the Dry Eye Symptom-Bother module.

The Dry Eye Symptom-Bother module of IDEEL is composed of a single dimension (20 items). A 4-point Likert-like scale is used: from "not at all" to "very much". Patients could also answer "I did not have this symptom / Not applicable". One item is scored on a 5-point Likert-like scale from "none of the time" to "all of the time". The range for the symptom-bother score is 0 to 100, with higher scores indicating greater symptom bother.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants in Cohort 2

End point values	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Participants	20	24		

Statistical analyses

Statistical analysis title	IDEEL up to Week 24 - Cohort 2
Comparison groups	Cohort 2/Arm F: Placebo v Cohort 2/Arm E: CFZ533 600 mg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5459
Method	Fisher exact
Parameter estimate	Clopper-Pearson method
Point estimate	8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	27.4

Secondary: Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods

End point title	Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods
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End point description:

The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters.

Analyses of data in the Safety Set (SAF) for period 2/3 or overall study is presented by actual treatment sequence during periods 1 and 2, where the CFZ533 600 mg – CFZ533 600 mg sequence included data from patients in separate cohort. CFZ533 600 mg 24 Weeks arm includes only patients from Placebo – CFZ533 600 mg arm, who took at least one CFZ533 600 mg dose in Period 2 (Patients who received Placebo in Period 1 and discontinued before Week 24 are not included). CFZ533 600 mg 48 Weeks arm includes all subjects from CFZ533 600 mg - CFZ533 600 mg arm, and subjects from CFZ533 150 mg - CFZ533 150 mg and CFZ533 300 mg - CFZ533 300 mg arms but only took the first or the first two loading dose(s) in period 1.

End point type	Secondary
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End point timeframe:

up to 14 weeks following the last dose of study treatment, up to maximum Week 60

End point values	Cohort 1: CFZ533 600 mg 24 Weeks	Cohort 1: CFZ533 150 mg 48 Weeks	Cohort 1: CFZ533 300 mg 48 Weeks	Cohort 1: CFZ533 600 mg 48 Weeks
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	44	42	44
Units: Participants				
Death	0	0	1	0
Adverse Event	34	40	38	43
Serious Adverse Event	4	6	6	6
AE leading to study medication discontinuation	0	2	3	5

End point values	Any CFZ533 600 mg	Any CFZ533		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	171		
Units: Participants				
Death	0	1		
Adverse Event	77	155		
Serious Adverse Event	10	22		
AE leading to study medication discontinuation	5	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24

End point title	Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24
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End point description:

The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters.

Analyses of data in the Safety Set (SAF) up to Week 24 (Period 1) is presented by actual treatment during Period 1, with data from separate cohort for the CFZ533 600mg and for the Placebo groups: CFZ533 600 mg and placebo.

End point type	Secondary
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End point timeframe:

Up to Week 24

End point values	Cohort 2: Placebo	Cohort 2: CFZ533 600 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: Participants				
Death	0	0		
Adverse Event	32	41		
Serious Adverse Event	2	2		
AE leading to study medication discontinuation	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods

End point title	Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods
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End point description:

The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters.

Analyses of data in the Safety Set (SAF) for period 2/3 or overall study is presented by actual treatment

sequence during periods 1 and 2, where the CFZ533 600 mg – CFZ533 600 mg sequence included data from patients in separate cohort. CFZ533 300 mg 24 Weeks includes only patients from Placebo - CFZ533 300 mg arm, who received Placebo in Period 1, and either took CFZ533 600 mg loading dose + at least two CFZ533 300 mg subsequent doses in Period 2 or missed CFZ533 600 mg loading dose and took at least one CFZ533 300 mg dose in Period 2 (Patients who received Placebo in Period 1 and discontinued before Week24 are not included). CFZ533 600 mg 48 Weeks arm includes all subjects from CFZ533 600 mg - CFZ533 600 mg arm.

End point type	Secondary
End point timeframe:	
up to 14 weeks following the last dose of study treatment, up to maximum Week 60	

End point values	Cohort 2: CFZ533 300 mg 24 Weeks	Cohort 2: CFZ533 600 mg 48 Weeks	Any CFZ533	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	50	94	
Units: Participants				
Death	0	1	1	
Adverse Event	35	44	79	
Serious Adverse Event	5	6	11	
AE leading to study medication discontinuation	0	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels

End point title	Cohort 1: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels
End point description:	
Serum samples for free light kappa (FLCκ) chains were collected and analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 40, Week 48 (End Treatment Period 2), FUP2 (Week 56), FUP 3 (Week 60)	

End point values	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	41	41	38
Units: mg/L				
least squares mean (standard error)				
Week 4	-1.9 (± 1.85)	-7.2 (± 1.86)	-5.4 (± 1.86)	-5.5 (± 1.92)
Week 12	-1.1 (± 2.02)	-9.7 (± 2.01)	-8.8 (± 2.03)	-8.6 (± 2.08)

Week 24 (End Treatment Period 1)	0.2 (± 2.26)	-9.9 (± 2.26)	-10.1 (± 2.28)	-11.3 (± 2.35)
Week 32	-8.6 (± 2.17)	-11.8 (± 2.17)	-11.1 (± 2.18)	-8.9 (± 2.26)
Week 40	-11.3 (± 2.05)	-12.0 (± 2.06)	-13.5 (± 2.07)	-11.0 (± 2.13)
Week 48 (End Treatment Period 2)	-13.9 (± 2.25)	-12.5 (± 2.25)	-13.1 (± 2.27)	-11.6 (± 2.32)
FUP2 (Week 56)	-11.8 (± 2.03)	-5.6 (± 1.99)	-8.9 (± 2.01)	-12.4 (± 2.06)
FUP 3 (Week 60)	-9.3 (± 2.07)	-3.9 (± 2.04)	-4.1 (± 2.07)	-10.3 (± 2.11)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels

End point title	Cohort 2: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels
End point description:	Serum samples for free light kappa (FLCκ) chains were collected and analyzed.
End point type	Secondary
End point timeframe:	Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 40, Week 48 (End Treatment Period 2), FUP2 (Week 56), FUP 3 (Week 60)

End point values	Cohort 2: Placebo - CFZ533 300 mg	Cohort 2: CFZ533 600 mg - CFZ533 600 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	49		
Units: mg/L				
least squares mean (standard error)				
Week 4	0.3 (± 0.92)	-4.3 (± 0.87)		
Week 12	0.1 (± 1.10)	-7.2 (± 1.06)		
Week 24 (End Treatment Period 1)	-0.2 (± 0.90)	-9.9 (± 0.86)		
Week 32	-6.0 (± 0.93)	-10.5 (± 0.89)		
Week 40	-7.8 (± 0.93)	-9.9 (± 0.91)		
Week 48 (End Treatment Period 2)	-9.3 (± 0.95)	-11.9 (± 0.92)		
FUP2 (Week 56)	-6.1 (± 1.00)	-11.7 (± 0.99)		
FUP 3 (Week 60)	-1.9 (± 1.11)	-11.0 (± 1.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Change from Baseline in Immunoglobulin G (IgG) levels

End point title	Cohort 1: Change from Baseline in Immunoglobulin G (IgG) levels
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End point description:

Plasma samples for Immunoglobulin G (IgG) were collected and analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)

End point values	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	43	43	43	41
Units: g/L				
least squares mean (standard error)				
Week 4	0.1 (± 0.31)	-0.9 (± 0.31)	-0.6 (± 0.31)	-0.8 (± 0.32)
Week 8	0.0 (± 0.31)	-1.1 (± 0.31)	-1.0 (± 0.31)	-1.4 (± 0.31)
Week 12	0.4 (± 0.28)	-1.7 (± 0.27)	-1.7 (± 0.28)	-1.5 (± 0.28)
Week 16	0.4 (± 0.39)	-1.8 (± 0.39)	-2.2 (± 0.39)	-2.0 (± 0.40)
Week 20	0.1 (± 0.35)	-2.4 (± 0.34)	-2.3 (± 0.35)	-2.1 (± 0.36)
Week 24 (End Treatment Period 1)	0.0 (± 0.36)	-2.1 (± 0.35)	-2.5 (± 0.36)	-2.5 (± 0.36)
Week 28	-0.9 (± 0.39)	-2.3 (± 0.38)	-2.7 (± 0.39)	-2.9 (± 0.39)
Week 32	-1.3 (± 0.36)	-2.6 (± 0.36)	-3.0 (± 0.36)	-3.3 (± 0.37)
Week 40	-2.3 (± 0.36)	-2.7 (± 0.36)	-3.2 (± 0.36)	-3.1 (± 0.36)
Week 48 (End Treatment Period 2)	-3.0 (± 0.40)	-2.8 (± 0.40)	-3.7 (± 0.41)	-3.4 (± 0.40)
FUP1 (Week 52)	-3.6 (± 0.47)	-2.9 (± 0.46)	-3.8 (± 0.47)	-3.7 (± 0.46)
FUP2 (Week 56)	-3.0 (± 0.45)	-2.0 (± 0.43)	-3.2 (± 0.44)	-3.9 (± 0.44)
FUP 3 (Week 60)	-2.9 (± 0.47)	-1.2 (± 0.46)	-1.9 (± 0.47)	-3.3 (± 0.46)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change from Baseline in Immunoglobulin G (IgG) levels

End point title	Cohort 2: Change from Baseline in Immunoglobulin G (IgG) levels
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End point description:

Plasma samples for Immunoglobulin G (IgG) were collected and analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)

End point values	Cohort 2: CFZ533 600 mg - CFZ533 600 mg	Cohort 2: Placebo - CFZ533 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	47		
Units: g/L				
least squares mean (standard error)				
Week 4	-0.8 (± 0.24)	-0.8 (± 0.25)		
Week 8	-1.9 (± 0.27)	-0.5 (± 0.28)		
Week 12	-2.5 (± 0.29)	-0.4 (± 0.30)		
Week 16	-3.0 (± 0.30)	-0.6 (± 0.32)		
Week 20	-3.2 (± 0.30)	-0.7 (± 0.32)		
Week 24 (End Treatment Period 1)	-3.6 (± 0.40)	0.0 (± 0.42)		
Week 28	-4.2 (± 0.36)	-1.3 (± 0.38)		
Week 32	-4.1 (± 0.34)	-1.5 (± 0.35)		
Week 40	-4.9 (± 0.42)	-2.6 (± 0.43)		
Week 48 (End Treatment Period 2)	-4.5 (± 0.43)	-3.2 (± 0.43)		
FUP1 (Week 52)	-5.0 (± 0.44)	-4.0 (± 0.45)		
FUP2 (Week 56)	-4.8 (± 0.45)	-3.3 (± 0.46)		
FUP 3 (Week 60)	-4.5 (± 0.45)	-2.4 (± 0.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Change from Baseline in Immunoglobulin M (IgM) levels

End point title	Cohort 1: Change from Baseline in Immunoglobulin M (IgM) levels
End point description:	Plasma samples for Immunoglobulin M (IgM) were collected and analyzed.
End point type	Secondary
End point timeframe:	Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)

End point values	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	43	43	43	41
Units: g/L				
least squares mean (standard error)				
Week 4	0.0 (± 0.04)	-0.1 (± 0.04)	-0.1 (± 0.04)	-0.1 (± 0.04)
Week 8	0.0 (± 0.04)	-0.2 (± 0.04)	-0.3 (± 0.04)	-0.2 (± 0.04)
Week 12	0.0 (± 0.04)	-0.2 (± 0.04)	-0.3 (± 0.04)	-0.2 (± 0.04)
Week 16	0.0 (± 0.05)	-0.2 (± 0.05)	-0.3 (± 0.05)	-0.3 (± 0.05)

Week 20	0.0 (± 0.05)	-0.2 (± 0.05)	-0.4 (± 0.05)	-0.3 (± 0.05)
Week 24 (End Treatment Period 1)	0.0 (± 0.06)	-0.2 (± 0.06)	-0.4 (± 0.06)	-0.3 (± 0.06)
Week 28	-0.1 (± 0.05)	-0.2 (± 0.05)	-0.4 (± 0.05)	-0.3 (± 0.05)
Week 32	-0.2 (± 0.06)	-0.2 (± 0.06)	-0.4 (± 0.06)	-0.3 (± 0.06)
Week 40	-0.3 (± 0.06)	-0.2 (± 0.06)	-0.4 (± 0.06)	-0.3 (± 0.06)
Week 48 (End Treatment Period 2)	-0.3 (± 0.06)	-0.2 (± 0.06)	-0.4 (± 0.06)	-0.3 (± 0.06)
FUP1 (Week 52)	-0.4 (± 0.05)	-0.2 (± 0.05)	-0.4 (± 0.05)	-0.3 (± 0.05)
FUP2 (Week 56)	-0.3 (± 0.05)	0.0 (± 0.05)	-0.1 (± 0.05)	-0.3 (± 0.05)
FUP 3 (Week 60)	-0.2 (± 0.07)	-0.1 (± 0.06)	0.0 (± 0.07)	-0.2 (± 0.06)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change from Baseline in Immunoglobulin M (IgM) levels

End point title	Cohort 2: Change from Baseline in Immunoglobulin M (IgM) levels
End point description:	
Plasma samples for Immunoglobulin M (IgM) were collected and analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)	

End point values	Cohort 2: CFZ533 600 mg - CFZ533 600 mg	Cohort 2: Placebo - CFZ533 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	47		
Units: g/L				
least squares mean (standard error)				
Week 4	-0.1 (± 0.03)	0.0 (± 0.03)		
Week 8	-0.3 (± 0.04)	0.0 (± 0.04)		
Week 12	-0.3 (± 0.05)	0.0 (± 0.05)		
Week 16	-0.4 (± 0.05)	-0.1 (± 0.06)		
Week 20	-0.4 (± 0.06)	-0.1 (± 0.06)		
Week 24 (End Treatment Period 1)	-0.4 (± 0.06)	0.0 (± 0.06)		
Week 28	-0.5 (± 0.06)	-0.2 (± 0.06)		
Week 32	-0.5 (± 0.06)	-0.2 (± 0.07)		
Week 40	-0.5 (± 0.07)	-0.3 (± 0.07)		
Week 48 (End Treatment Period 2)	-0.5 (± 0.07)	-0.3 (± 0.07)		
FUP1 (Week 52)	-0.5 (± 0.06)	-0.3 (± 0.06)		
FUP2 (Week 56)	-0.5 (± 0.07)	-0.2 (± 0.72)		
FUP 3 (Week 60)	-0.5 (± 0.08)	-0.1 (± 0.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Change from Baseline in plasma CXCL-13 levels

End point title	Cohort 1: Change from Baseline in plasma CXCL-13 levels
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End point description:

Plasma samples for Chemokine (C-X-C motif) ligand 13 (CXCL13), also known as B lymphocyte chemoattractant (BLC) or B cell-attracting chemokine 1 (BCA-1) were collected and analyzed.

End point type	Secondary
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End point timeframe:

Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 48 (End Treatment Period 2), FUP 3 (Week 60)

End point values	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	43	40	39
Units: pg/mL				
least squares mean (standard error)				
Week 4	-88.4 (± 12.74)	-19.0 (± 12.51)	-78.7 (± 12.84)	-77.0 (± 13.23)
Week 12	-77.4 (± 12.59)	-23.8 (± 12.42)	-99.4 (± 12.56)	-108.5 (± 12.69)
Week 24 (End Treatment Period 1)	-83.2 (± 13.98)	-15.6 (± 13.78)	-89.7 (± 14.08)	-111.6 (± 14.26)
Week 32	-78.3 (± 18.21)	-102.5 (± 17.37)	-80.5 (± 17.68)	-71.3 (± 19.02)
Week 48 (End Treatment Period 2)	-89.7 (± 12.26)	-116.6 (± 11.73)	-75.9 (± 12.02)	-118.7 (± 12.15)
FUP 3 (Week 60)	-22.4 (± 22.55)	-73.9 (± 21.62)	24.4 (± 22.10)	-68.7 (± 22.24)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Change from Baseline in plasma CXCL-13 levels

End point title	Cohort 2: Change from Baseline in plasma CXCL-13 levels
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End point description:

Plasma samples for Chemokine (C-X-C motif) ligand 13 (CXCL13), also known as B lymphocyte

chemoattractant (BLC) or B cell-attracting chemokine 1 (BCA-1) were collected and analyzed.

End point type	Secondary
End point timeframe:	
Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 48 (End Treatment Period 2), FUP 3 (Week 60)	

End point values	Cohort 2: CFZ533 600 mg - CFZ533 600 mg	Cohort 2: Placebo - CFZ533 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	45		
Units: pg/mL				
least squares mean (standard error)				
Week 4	-88.7 (± 7.99)	-9.0 (± 8.50)		
Week 12	-97.8 (± 15.55)	8.8 (± 16.16)		
Week 24 (End Treatment Period 1)	-114.1 (± 6.81)	-27.4 (± 7.19)		
Week 32	-116.1 (± 6.65)	-97.2 (± 7.03)		
Week 48 (End Treatment Period 2)	-107.8 (± 6.81)	-99.2 (± 6.84)		
FUP 3 (Week 60)	-66.5 (± 10.53)	-10.9 (± 10.76)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment adverse events and deaths were reported from first dose of study treatment to 14 weeks after last dose of study medication, up to Week 60.

Adverse event reporting additional description:

Any sign or symptom that occurred during the conduct of the trial and safety follow-up. The safety analysis 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Cohort 1@Placebo@24 Weeks
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Reporting group description:

Cohort 1@Placebo@24 Weeks

Reporting group title	Cohort 1@CFZ533 600 mg@24 Weeks
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Reporting group description:

Cohort 1@CFZ533 600 mg@24 Weeks

Reporting group title	Cohort 1@CFZ533 150 mg@48 Weeks
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Reporting group description:

Cohort 1@CFZ533 150 mg@48 Weeks

Reporting group title	Cohort 1@CFZ533 300 mg@48 Weeks
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Reporting group description:

Cohort 1@CFZ533 300 mg@48 Weeks

Reporting group title	Cohort 1@CFZ533 600 mg@48 Weeks
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Reporting group description:

Cohort 1@CFZ533 600 mg@48 Weeks

Reporting group title	Cohort 2@Placebo@24 Weeks
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Reporting group description:

Cohort 2@Placebo@24 Weeks

Reporting group title	Cohort 2@CFZ533 300 mg@24 Weeks
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Reporting group description:

Cohort 2@CFZ533 300 mg@24 Weeks

Reporting group title	Cohort 2@CFZ533 600 mg@48 Weeks
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Reporting group description:

Cohort 2@CFZ533 600 mg@48 Weeks

Serious adverse events	Cohort 1@Placebo@24 Weeks	Cohort 1@CFZ533 600 mg@24 Weeks	Cohort 1@CFZ533 150 mg@48 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)	4 / 41 (9.76%)	6 / 44 (13.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic organ prolapse			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			

subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebrovascular disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland cyst			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Hand deformity			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sjogren's syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis bacterial			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumocystis jirovecii pneumonia subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal abscess subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound abscess subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 1@CFZ533 300 mg@48 Weeks	Cohort 1@CFZ533 600 mg@48 Weeks	Cohort 2@Placebo@24 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 42 (14.29%)	6 / 44 (13.64%)	2 / 50 (4.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from	1	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic organ prolapse			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			

subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebrovascular disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			

subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland cyst			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Hand deformity			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sjogren's syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis bacterial			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumocystis jirovecii pneumonia subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal abscess subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound abscess subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2@CFZ533 300 mg@24 Weeks	Cohort 2@CFZ533 600 mg@48 Weeks	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 44 (11.36%)	6 / 50 (12.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 44 (2.27%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic organ prolapse			
subjects affected / exposed	1 / 44 (2.27%)	0 / 50 (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			
Dyspnoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			

subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 44 (2.27%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Cerebrovascular disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
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			
Anaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			

subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland cyst			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Hand deformity			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren's syndrome			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis bacterial			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumocystis jirovecii pneumonia subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia subjects affected / exposed	1 / 44 (2.27%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral subjects affected / exposed	1 / 44 (2.27%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1@Placebo@24 Weeks	Cohort 1@CFZ533 600 mg@24 Weeks	Cohort 1@CFZ533 150 mg@48 Weeks
Total subjects affected by non-serious adverse events subjects affected / exposed	18 / 43 (41.86%)	28 / 41 (68.29%)	33 / 44 (75.00%)
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	0 / 41 (0.00%) 0	3 / 44 (6.82%) 3
Immunisation reaction subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 2	3 / 41 (7.32%) 4	1 / 44 (2.27%) 1
Vascular disorders Haematoma subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 41 (0.00%) 0	0 / 44 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	4 / 43 (9.30%) 4	0 / 41 (0.00%) 0	2 / 44 (4.55%) 2
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	0 / 41 (0.00%) 0	2 / 44 (4.55%) 2
Headache subjects affected / exposed occurrences (all)	5 / 43 (11.63%) 6	1 / 41 (2.44%) 1	9 / 44 (20.45%) 16
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 41 (2.44%) 1	0 / 44 (0.00%) 0
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 41 (2.44%) 1	1 / 44 (2.27%) 1
Neutropenia subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 41 (0.00%) 0	0 / 44 (0.00%) 0
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 41 (2.44%) 3	1 / 44 (2.27%) 3
Fatigue subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 41 (2.44%) 1	5 / 44 (11.36%) 5
Pyrexia subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 3	2 / 41 (4.88%) 2	6 / 44 (13.64%) 6
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 41 (2.44%) 1	1 / 44 (2.27%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 41 (0.00%) 0	1 / 44 (2.27%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	0 / 41 (0.00%) 0	1 / 44 (2.27%) 1
Diarrhoea subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 41 (2.44%) 1	2 / 44 (4.55%) 3
Nausea subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 41 (0.00%) 0	2 / 44 (4.55%) 2
Parotid gland enlargement subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 41 (0.00%) 0	0 / 44 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 41 (0.00%) 0	2 / 44 (4.55%) 2
Cough subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 41 (2.44%) 1	3 / 44 (6.82%) 3

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 43 (0.00%)	2 / 41 (4.88%)	1 / 44 (2.27%)
occurrences (all)	0	3	1
Pruritus			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Eczema			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	3
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 43 (9.30%)	2 / 41 (4.88%)	6 / 44 (13.64%)
occurrences (all)	5	4	7
Back pain			
subjects affected / exposed	1 / 43 (2.33%)	2 / 41 (4.88%)	4 / 44 (9.09%)
occurrences (all)	1	2	4
Neck pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 41 (2.44%)	1 / 44 (2.27%)
occurrences (all)	1	1	1
Pain in extremity			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	2
Infections and infestations			
COVID-19			

subjects affected / exposed	2 / 43 (4.65%)	10 / 41 (24.39%)	10 / 44 (22.73%)
occurrences (all)	2	10	11
Conjunctivitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	4 / 44 (9.09%)
occurrences (all)	1	0	5
Influenza			
subjects affected / exposed	0 / 43 (0.00%)	3 / 41 (7.32%)	2 / 44 (4.55%)
occurrences (all)	0	3	2
Pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	2 / 43 (4.65%)	0 / 41 (0.00%)	3 / 44 (6.82%)
occurrences (all)	2	0	4
Nasopharyngitis			
subjects affected / exposed	2 / 43 (4.65%)	6 / 41 (14.63%)	5 / 44 (11.36%)
occurrences (all)	2	6	8
Rhinitis			
subjects affected / exposed	1 / 43 (2.33%)	1 / 41 (2.44%)	0 / 44 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 43 (2.33%)	4 / 41 (9.76%)	3 / 44 (6.82%)
occurrences (all)	1	4	4
Sinusitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	1 / 44 (2.27%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	2 / 43 (4.65%)	3 / 41 (7.32%)	3 / 44 (6.82%)
occurrences (all)	3	5	5

Non-serious adverse events	Cohort 1@CFZ533 300 mg@48 Weeks	Cohort 1@CFZ533 600 mg@48 Weeks	Cohort 2@Placebo@24 Weeks
Total subjects affected by non-serious adverse events			

subjects affected / exposed	34 / 42 (80.95%)	34 / 44 (77.27%)	27 / 50 (54.00%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Immunisation reaction			
subjects affected / exposed	3 / 42 (7.14%)	1 / 44 (2.27%)	0 / 50 (0.00%)
occurrences (all)	3	1	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 42 (0.00%)	3 / 44 (6.82%)	0 / 50 (0.00%)
occurrences (all)	0	4	0
Hypertension			
subjects affected / exposed	0 / 42 (0.00%)	2 / 44 (4.55%)	3 / 50 (6.00%)
occurrences (all)	0	3	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 42 (7.14%)	4 / 44 (9.09%)	2 / 50 (4.00%)
occurrences (all)	4	6	2
Headache			
subjects affected / exposed	6 / 42 (14.29%)	8 / 44 (18.18%)	5 / 50 (10.00%)
occurrences (all)	8	15	7
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 42 (7.14%)	2 / 44 (4.55%)	0 / 50 (0.00%)
occurrences (all)	3	4	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	5 / 42 (11.90%)	2 / 44 (4.55%)	0 / 50 (0.00%)
occurrences (all)	6	4	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 42 (4.76%)	3 / 44 (6.82%)	0 / 50 (0.00%)
occurrences (all)	2	4	0
Fatigue			

subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	3 / 44 (6.82%) 5	0 / 50 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 5	0 / 44 (0.00%) 0	0 / 50 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 44 (2.27%) 1	0 / 50 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	4 / 44 (9.09%) 6	1 / 50 (2.00%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 6	0 / 44 (0.00%) 0	0 / 50 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	3 / 44 (6.82%) 6	5 / 50 (10.00%) 6
Nausea subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	2 / 44 (4.55%) 4	3 / 50 (6.00%) 3
Parotid gland enlargement subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 4	0 / 44 (0.00%) 0	0 / 50 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 3	1 / 44 (2.27%) 1	1 / 50 (2.00%) 1
Cough subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 3	2 / 44 (4.55%) 3	2 / 50 (4.00%) 2
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	3 / 44 (6.82%) 4	2 / 50 (4.00%) 2

Rash			
subjects affected / exposed	2 / 42 (4.76%)	1 / 44 (2.27%)	4 / 50 (8.00%)
occurrences (all)	2	1	5
Pruritus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	3 / 50 (6.00%)
occurrences (all)	0	1	3
Eczema			
subjects affected / exposed	1 / 42 (2.38%)	3 / 44 (6.82%)	2 / 50 (4.00%)
occurrences (all)	1	3	2
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 42 (4.76%)	5 / 44 (11.36%)	4 / 50 (8.00%)
occurrences (all)	2	8	4
Back pain			
subjects affected / exposed	3 / 42 (7.14%)	1 / 44 (2.27%)	3 / 50 (6.00%)
occurrences (all)	4	1	3
Neck pain			
subjects affected / exposed	0 / 42 (0.00%)	3 / 44 (6.82%)	0 / 50 (0.00%)
occurrences (all)	0	3	0
Myalgia			
subjects affected / exposed	3 / 42 (7.14%)	2 / 44 (4.55%)	1 / 50 (2.00%)
occurrences (all)	3	3	2
Pain in extremity			
subjects affected / exposed	1 / 42 (2.38%)	3 / 44 (6.82%)	1 / 50 (2.00%)
occurrences (all)	2	3	1
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 42 (26.19%)	11 / 44 (25.00%)	8 / 50 (16.00%)
occurrences (all)	11	13	8
Conjunctivitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	3 / 50 (6.00%)
occurrences (all)	0	1	3

Herpes simplex subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 44 (2.27%) 1	0 / 50 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 5	2 / 44 (4.55%) 3	0 / 50 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	1 / 44 (2.27%) 2	0 / 50 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 4	5 / 44 (11.36%) 11	1 / 50 (2.00%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 42 (19.05%) 13	9 / 44 (20.45%) 11	3 / 50 (6.00%) 6
Rhinitis subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	2 / 44 (4.55%) 2	2 / 50 (4.00%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 3	1 / 44 (2.27%) 1	1 / 50 (2.00%) 2
Sinusitis subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2	1 / 44 (2.27%) 1	2 / 50 (4.00%) 2
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 4	5 / 44 (11.36%) 10	0 / 50 (0.00%) 0

Non-serious adverse events	Cohort 2@CFZ533 300 mg@24 Weeks	Cohort 2@CFZ533 600 mg@48 Weeks	
Total subjects affected by non-serious adverse events subjects affected / exposed	32 / 44 (72.73%)	41 / 50 (82.00%)	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	1 / 50 (2.00%) 1	
Immunisation reaction			

subjects affected / exposed occurrences (all)	0 / 44 (0.00%) 0	0 / 50 (0.00%) 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	2 / 44 (4.55%)	2 / 50 (4.00%)	
occurrences (all)	2	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 44 (4.55%)	0 / 50 (0.00%)	
occurrences (all)	9	0	
Headache			
subjects affected / exposed	4 / 44 (9.09%)	3 / 50 (6.00%)	
occurrences (all)	4	4	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 50 (4.00%)	
occurrences (all)	0	2	
Iron deficiency anaemia			
subjects affected / exposed	1 / 44 (2.27%)	3 / 50 (6.00%)	
occurrences (all)	1	3	
Neutropenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 44 (2.27%)	2 / 50 (4.00%)	
occurrences (all)	1	2	
Pyrexia			
subjects affected / exposed	2 / 44 (4.55%)	4 / 50 (8.00%)	
occurrences (all)	2	6	

Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 2	3 / 50 (6.00%) 3	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Parotid gland enlargement subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1 2 / 44 (4.55%) 2 1 / 44 (2.27%) 1 1 / 44 (2.27%) 1 0 / 44 (0.00%) 0	2 / 50 (4.00%) 2 2 / 50 (4.00%) 2 4 / 50 (8.00%) 4 4 / 50 (8.00%) 7 0 / 50 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	0 / 44 (0.00%) 0 1 / 44 (2.27%) 1	0 / 50 (0.00%) 0 3 / 50 (6.00%) 4	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Pruritus	0 / 44 (0.00%) 0 0 / 44 (0.00%) 0	3 / 50 (6.00%) 3 6 / 50 (12.00%) 7	

subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all)	0 / 44 (0.00%) 0 1 / 44 (2.27%) 1	3 / 50 (6.00%) 4 3 / 50 (6.00%) 4	
Endocrine disorders Thyroid mass subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	3 / 50 (6.00%) 3	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	5 / 44 (11.36%) 6 6 / 44 (13.64%) 6 2 / 44 (4.55%) 2 1 / 44 (2.27%) 2 2 / 44 (4.55%) 2	5 / 50 (10.00%) 6 6 / 50 (12.00%) 7 0 / 50 (0.00%) 0 4 / 50 (8.00%) 5 4 / 50 (8.00%) 5	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Herpes simplex subjects affected / exposed occurrences (all) Influenza	8 / 44 (18.18%) 8 2 / 44 (4.55%) 2 0 / 44 (0.00%) 0	20 / 50 (40.00%) 22 1 / 50 (2.00%) 1 3 / 50 (6.00%) 3	

subjects affected / exposed	2 / 44 (4.55%)	1 / 50 (2.00%)	
occurrences (all)	2	1	
Pneumonia			
subjects affected / exposed	0 / 44 (0.00%)	3 / 50 (6.00%)	
occurrences (all)	0	3	
Oral herpes			
subjects affected / exposed	4 / 44 (9.09%)	1 / 50 (2.00%)	
occurrences (all)	4	2	
Nasopharyngitis			
subjects affected / exposed	3 / 44 (6.82%)	6 / 50 (12.00%)	
occurrences (all)	4	6	
Rhinitis			
subjects affected / exposed	1 / 44 (2.27%)	5 / 50 (10.00%)	
occurrences (all)	2	6	
Upper respiratory tract infection			
subjects affected / exposed	3 / 44 (6.82%)	6 / 50 (12.00%)	
occurrences (all)	4	11	
Sinusitis			
subjects affected / exposed	1 / 44 (2.27%)	4 / 50 (8.00%)	
occurrences (all)	1	4	
Urinary tract infection			
subjects affected / exposed	4 / 44 (9.09%)	8 / 50 (16.00%)	
occurrences (all)	5	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 February 2020	Amendment 1: Introduction of screening for human cytomegalovirus (CMV) and monitoring for active CMV infection in at risk subjects.
27 April 2021	Amendment 2: Introduction of an interim analysis to assess the dose response relationship of iscalimab, after at least 50% of the subjects in Cohort 1 have completed Week 24 visit or discontinued prior to that. The results from the interim analysis may inform future clinical development planning.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported