Clinical trial results:
Investigator- and subject-blinded, randomized, placebo-controlled study to
evaluate safety, tolerability, pharmacokinetics and efficacy trial of CFZ533 in
pediatric and young adult subjects with new onset type 1 diabetes (T1DM)

Summary

EudraCT number	2018-004553-25
Trial protocol	BE SI DE IT
Global end of trial date	04 June 2024

Results information

Result version number	v2 (current)
This version publication date	02 February 2025
First version publication date	18 December 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CCFZ533X2207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04129528
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives:
- To evaluate effects of CFZ533 on pancreatic beta cell function in subjects with new-onset Type 1 Diabetes Mellitus (T1DM).
- To evaluate the safety and tolerability of CFZ533 in subjects with new onset T1DM.

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	08 November 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	Belgium: 13
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Slovenia: 1
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	44
EEA total number of subjects	42

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)	35
Adults (18-64 years)	9
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 12 investigative sites in 6 countries.

Pre-assignment

Screening details:

Enrolment was based on both screening and baseline results. The screening and baseline visit(s) may be conducted over 1 or more visits depending on the subject's body weight and World Health Organization and European Medicines Agency (EMA) recommendations for trial related phlebotomy limits.

Period 1

Period 1 title	Overall Study (overall period)
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
Arm title	CFZ533

Arm description:

CFZ533 30 mg/kg i.v. dose on Day 1. From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg received 195 mg s.c., and participants with body weight of ≥ 50 kg to ≤125 kg received 300 mg s.c. on a weekly basis.

Arm type	Experimental
Investigational medicinal product name	CFZ533
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CFZ533 30 mg/kg i.v. dose on Day 1.

Investigational medicinal product name	CFZ533
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

CFZ533 From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg received 195 mg s.c., and participants with body weight of ≥ 50 kg to ≤125 kg received 300 mg s.c. on a weekly basis.

Arm title	Placebo

Arm description:

Placebo i.v. dose on Day 1. From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg and body weight of ≥ 50 kg to ≤125 kg received matching placebo s.c. on a weekly basis.

Arm type	Placebo
Investigational medicinal product name	CFZ533
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details: Placebo From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg and body weight of ≥ 50 kg to ≤125 kg received matching placebo s.c. on a weekly basis.	
Investigational medicinal product name	CFZ533
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Placebo i.v. dose on Day 1.	

Number of subjects in period 1	CFZ533	Placebo
Started	29	15
Completed	26	13
Not completed	3	2
Consent withdrawn by subject	1	1
Physician decision	1	1
Adverse event	1	-

Baseline characteristics

Reporting groups	
Reporting group title	CFZ533
Reporting group description:	
CFZ533 30 mg/kg i.v. dose on Day 1. From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg received 195 mg s.c., and participants with body weight of ≥ 50 kg to ≤125 kg received 300 mg s.c. on a weekly basis.	
Reporting group title	Placebo
Reporting group description:	
Placebo i.v. dose on Day 1. From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg and body weight of ≥ 50 kg to ≤125 kg received matching placebo s.c. on a weekly basis.	

Reporting group values	CFZ533	Placebo	Total
Number of subjects	29	15	44
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)	23	12	35
Adults (18-64 years)	6	3	9
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	15.6	15.5	
standard deviation	± 2.81	± 3.07	-
Sex: Female, Male			
Units: participants			
Female	10	5	15
Male	19	10	29
Race/Ethnicity, Customized			
Units: Subjects			
White	29	15	44

End points

End points reporting groups

Reporting group title	CFZ533
Reporting group description:	
CFZ533 30 mg/kg i.v. dose on Day 1. From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg received 195 mg s.c., and participants with body weight of ≥ 50 kg to ≤125 kg received 300 mg s.c. on a weekly basis.	
Reporting group title	Placebo
Reporting group description:	
Placebo i.v. dose on Day 1. From Day 8 up to Day 358 participants with body weight of ≥30 to <50 kg and body weight of ≥ 50 kg to ≤125 kg received matching placebo s.c. on a weekly basis.	

Primary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs) during the on-treatment period

End point title	Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs) during the on-treatment period[1]
End point description:	
Number of participants with treatment emergent AEs (any AE regardless of seriousness), AEs led to study treatment discontinuation, and SAEs. On-treatment period is defined as from date of first administration of study treatment to 98 days after date of last administration of study treatment (including start and stop date).	
End point type	Primary
End point timeframe:	
Adverse events were reported from first dose of study treatment to 98 days after last dose, up to a maximum duration of approximately 65 weeks	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: only analyzed descriptively.	

End point values	CFZ533	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: participants				
Adverse Events	28	13		
Serious Adverse Events	4	1		
AEs leading to discontinuation of study treatment	4	0		

Statistical analyses

No statistical analyses for this end point

Primary: Normalized stimulated C-peptide area under the curve (AUC) at Week 52

End point title	Normalized stimulated C-peptide area under the curve (AUC) at Week 52

End point description:

The mixed meal tolerance test (MMTT) has appropriate sensitivity to detect residual insulin secretion and beta cell function. In the MMTT, following an 8-10 hour overnight fast, a weight-based liquid meal provided as 6 mL/kg (maximum 360 mL) of mixed meal, ingested over 5 min with timed blood samples for glucose and C peptide determination obtained 10 min prior to ingestion (t = −10), at baseline (t = 0), and at 15, 30, 60, 90, and 120 min after consumption of the liquid meal. The time collections for post load samples are based on the start time of the mixed meal.
Stimulated C-peptide AUC by the standard MMTT, normalized by the duration of measurements, was analyzed with a mixed model repeated measures analysis.

End point type	Primary

End point timeframe:

At Week 52, 10 min prior to ingestion, at start of ingestion, and at 15, 30, 60, 90, and 120 min after consumption of the liquid meal.

End point values	CFZ533	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: nmol/L				
geometric mean (confidence interval 80%)	0.42 (0.36 to 0.49)	0.36 (0.30 to 0.44)		

Statistical analyses

Statistical analysis title	Normalized stimulated C-peptide AUC
Comparison groups	CFZ533 v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1817 [2]
Method	Mixed model repeated measure analysis
Parameter estimate	Ratio of geometric means CFZ533/placebo
Point estimate	1.173
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.94
upper limit	1.47

Notes:

[2] - one-sided P-value

Secondary: Maximum plasma concentration (Cmax) of CFZ533 after intravenous (IV) administration

End point title	Maximum plasma concentration (Cmax) of CFZ533 after intravenous (IV) administration[3]

End point description:

Cmax is defined as the maximum (peak) observed concentration following a dose. Free CFZ533 plasma concentrations were determined using a validated target-based sandwich enzyme-linked immunosorbent assay (ELISA) method.

End point type	Secondary

End point timeframe:

Day 1: Pre-dose and 90 minutes after the start of the IV infusion (duration of the infusion is 30 minutes).

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: PK Endpoint not analyzed for participants on placebo

End point values	CFZ533			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: ug/mL				
arithmetic mean (standard deviation)	506 (± 124)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough plasma concentration (Ctrough) of CFZ533

End point title	Trough plasma concentration (Ctrough) of CFZ533[4]

End point description:

Ctrough is the observed plasma concentration that is just prior to the beginning of, or at the end of a dosing interval. Free CFZ533 plasma concentrations were determined using a validated target-based sandwich ELISA method. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Pre-dose at: Day 1, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72.

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: PK Endpoint not analyzed for participants on placebo

End point values	CFZ533			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: ug/mL				
arithmetic mean (standard deviation)				
Day 1 (n=27)	0.00 (± 0.00)			
Week 4 (n=26)	182 (± 40.9)			
Week 8 (n=25)	171 (± 45.8)			
Week 12 (n=21)	169 (± 43.1)			
Week 16 (n=18)	193 (± 55.2)			
Week 20 (n=20)	184 (± 68.1)			
Week 24 (n=16)	176 (± 65.2)			
Week 28 (n=18)	186 (± 61.4)			
Week 32 (n=16)	177 (± 65.4)			
Week 36 (n=17)	180 (± 86.7)			
Week 40 (n=15)	183 (± 80.0)			
Week 44 (n=14)	170 (± 88.7)			

Week 48 (n=15)	205 (± 101)			
Week 52 (n=29)	155 (± 111)			
Week 56 (n=26)	72.6 (± 53.3)			
Week 60 (n=25)	30.9 (± 24.9)			
Week 64 (n=26)	9.23 (± 11.7)			
Week 68 (n=25)	1.86 (± 3.15)			
Week 72 (n=26)	0.221 (± 0.499)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum plasma concentration (Tmax) of CFZ533 after IV administration

End point title	Time to reach maximum plasma concentration (Tmax) of CFZ533 after IV administration[5]

End point description:

Tmax is the time to reach maximum (peak) drug concentration after single-dose administration (time). Free CFZ533 plasma concentrations were determined using a validated target-based sandwich ELISA method. Theoretical sampling time points were used to report Tmax.

End point type	Secondary

End point timeframe:

Day 1: Pre-dose and 90 minutes after the start of the IV infusion (duration of the infusion is 30 minutes).

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: PK Endpoint not analyzed for participants on placebo

End point values	CFZ533			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: hours				
median (full range (min-max))	1.5 (1.5 to 1.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with full or partial remission

End point title	Number of participants with full or partial remission

End point description:

Full remission is defined by HbA1c ≤ 6.5% (48 mmol/mol) and no exogenous insulin use at Week 52.
Partial remission 1 is defined by Insulin Dose Adjusted HbA1c (IDAA1c) ≤ 9.0 at Week 52.
Partial remission 2 is defined by HbA1c < 7.0% (53 mmol/mol) and total daily insulin dose <0.5 units per kg per day at Week 52.
Two different criteria for partial remission were considered, and patients were assessed separately according to each criterion.

End point type	Secondary

End point timeframe:

Week 52

End point values	CFZ533	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: participants				
Full remission	0	0		
Partial remission 1	20	10		
Partial remission 2	15	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Normalized stimulated C-peptide area under the curve (AUC) at Week 72

End point title	Normalized stimulated C-peptide area under the curve (AUC) at Week 72

End point description:

The mixed meal tolerance test (MMTT) has appropriate sensitivity to detect residual insulin secretion and beta cell function. In the MMTT, following an 8-10 hour overnight fast, a weight-based liquid meal provided as 6 mL/kg (maximum 360 mL) of mixed meal, ingested over 5 min with timed blood samples for glucose and C peptide determination obtained 10 min prior to ingestion (t = −10), at baseline (t = 0), and at 15, 30, 60, 90, and 120 min after consumption of the liquid meal. The time collections for post load samples are based on the start time of the mixed meal.
Stimulated C-peptide AUC by the standard MMTT, normalized by the duration of measurements, was analyzed with a mixed model repeated measures analysis.

End point type	Secondary

End point timeframe:

At Week 72, 10 min prior to ingestion, at start of ingestion, and at 15, 30, 60, 90, and 120 min after consumption of the liquid meal.

End point values	CFZ533	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: nmol/L				
geometric mean (confidence interval 80%)	0.40 (0.34 to 0.47)	0.32 (0.26 to 0.39)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of approximately 72 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	CFZ533

Reporting group description:

CFZ533

Reporting group title	Total

Reporting group description:

Total

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	CFZ533	Total	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 29 (20.69%)	7 / 44 (15.91%)	1 / 15 (6.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Traumatic fracture			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tonic clonic movements			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Large intestine infection			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 29 (3.45%)	1 / 44 (2.27%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CFZ533	Total	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 29 (93.10%)	41 / 44 (93.18%)	14 / 15 (93.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Medical device pain			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Pyrexia			
subjects affected / exposed	5 / 29 (17.24%)	8 / 44 (18.18%)	3 / 15 (20.00%)
occurrences (all)	6	10	4
Asthenia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	2	3	1
Injection site reaction			
subjects affected / exposed	7 / 29 (24.14%)	10 / 44 (22.73%)	3 / 15 (20.00%)
occurrences (all)	39	114	75
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Oropharyngeal pain			

subjects affected / exposed	3 / 29 (10.34%)	4 / 44 (9.09%)	1 / 15 (6.67%)
occurrences (all)	4	5	1
Dyspnoea			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	1 / 29 (3.45%)	5 / 44 (11.36%)	4 / 15 (26.67%)
occurrences (all)	4	8	4
Bronchial hyperreactivity			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Asthma			
subjects affected / exposed	0 / 29 (0.00%)	2 / 44 (4.55%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Rhinorrhoea			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	5	5
Nasal congestion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 29 (3.45%)	3 / 44 (6.82%)	2 / 15 (13.33%)
occurrences (all)	1	3	2
Lipids increased			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Serology positive			

subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Urine analysis abnormal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	2	2
Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	2	8	6
Limb injury			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Muscle strain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Congenital, familial and genetic disorders			
Gilbert's syndrome			
subjects affected / exposed	0 / 29 (0.00%)	2 / 44 (4.55%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 29 (24.14%)	9 / 44 (20.45%)	2 / 15 (13.33%)
occurrences (all)	14	16	2
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	4 / 29 (13.79%)	4 / 44 (9.09%)	0 / 15 (0.00%)
occurrences (all)	4	4	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 29 (17.24%)	6 / 44 (13.64%)	1 / 15 (6.67%)
occurrences (all)	6	7	1
Abdominal pain upper			

subjects affected / exposed	2 / 29 (6.90%)	4 / 44 (9.09%)	2 / 15 (13.33%)
occurrences (all)	2	4	2
Vomiting			
subjects affected / exposed	3 / 29 (10.34%)	3 / 44 (6.82%)	0 / 15 (0.00%)
occurrences (all)	3	3	0
Odynophagia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	4	3
Nausea			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Diarrhoea			
subjects affected / exposed	4 / 29 (13.79%)	4 / 44 (9.09%)	0 / 15 (0.00%)
occurrences (all)	9	9	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Dermatitis atopic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	2	2
Acne			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Ingrowing nail			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 29 (24.14%)	9 / 44 (20.45%)	2 / 15 (13.33%)
occurrences (all)	7	9	2
Chronic active Epstein-Barr virus infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Cytomegalovirus infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Epstein-Barr virus infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Gastroenteritis			
subjects affected / exposed	3 / 29 (10.34%)	5 / 44 (11.36%)	2 / 15 (13.33%)
occurrences (all)	3	8	5
Gastroenteritis viral			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	3 / 29 (10.34%)	6 / 44 (13.64%)	3 / 15 (20.00%)
occurrences (all)	4	7	3
Nasopharyngitis			
subjects affected / exposed	13 / 29 (44.83%)	18 / 44 (40.91%)	5 / 15 (33.33%)
occurrences (all)	33	42	9
Otitis externa			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	2	3	1
Parvovirus B19 infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Pharyngitis			

subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	3	2
Pharyngotonsillitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 44 (4.55%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Respiratory tract infection			
subjects affected / exposed	3 / 29 (10.34%)	3 / 44 (6.82%)	0 / 15 (0.00%)
occurrences (all)	7	7	0
Rhinitis			
subjects affected / exposed	2 / 29 (6.90%)	4 / 44 (9.09%)	2 / 15 (13.33%)
occurrences (all)	2	5	3
Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 44 (2.27%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Tinea pedis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Tonsillitis			
subjects affected / exposed	0 / 29 (0.00%)	3 / 44 (6.82%)	3 / 15 (20.00%)
occurrences (all)	0	4	4
Tooth abscess			
subjects affected / exposed	0 / 29 (0.00%)	2 / 44 (4.55%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 29 (13.79%)	7 / 44 (15.91%)	3 / 15 (20.00%)
occurrences (all)	9	12	3
Urinary tract infection			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Viral infection			
subjects affected / exposed	2 / 29 (6.90%)	2 / 44 (4.55%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 44 (4.55%)	1 / 15 (6.67%)
occurrences (all)	1	2	1

Hypoglycaemia subjects affected / exposed occurrences (all)	19 / 29 (65.52%) 181	27 / 44 (61.36%) 285	8 / 15 (53.33%) 104

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2019	This protocol amendment addresses comments received from Federal Agency for Medicines and Health Products in the letter dated 08July2019.
10 December 2019	The purpose of this amendment was to include additional safety monitoring that has already been implemented via urgent safety measures (USMs) in response to a suspected unexpected serious adverse reaction that was reported in another CFZ533 study of lupus nephritis patients.
30 November 2020	The purpose of this amendment was to include additional safety monitoring in response to the newly prevalent community exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
04 January 2021	Based on comments by the MHRA, the age classifications in the Cohorts have been revised to be more in line with International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Topic E11 age classifications.
17 March 2022	The purpose of this amendment was to implement a Hybrid Trial Design which included a flexible model for incorporating both on-site (traditional on-site based) and off-site (also known as remote or decentralized) elements within the same study design.
03 April 2023	The purpose of this protocol amendment was primarily to reduce the sample size and duration of study conduct.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 March 2020	There was a temporary halt implemented for both recruitment and treatment of participants on 16-Mar-2020 due to the COVID-19 worldwide pandemic with the trial approved to restart on 27-Aug-2020 based on country and site feasibility coming out of COVID-19.	27 August 2020

Notes:

Limitations and caveats

None reported