Clinical trial results:
A Phase Ib/IIa, Open-Label, Multicenter Clinical Trial to Assess Safety and Efficacy of the Human Anti-CD38 Antibody MOR202 in anti-PLA2R antibody positive Membranous Nephropathy (aMN) - M-PLACE

Summary

EudraCT number	2019-000780-24
Trial protocol	NL ES BE FR IT PL
Global end of trial date	02 August 2022

Results information

Result version number	v1 (current)
This version publication date	16 August 2023
First version publication date	16 August 2023

Trial information

Trial identification

Sponsor protocol code	MOR202C103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04145440
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hi-Bio
Sponsor organisation address	6000 Shoreline Court, Suite 304, South San Francisco, California, United States, 94080
Public contact	HI-Bio Clinical Program Lead, Hi-Bio, 1 408-548-7261, clinicaltrialdisclosure@hibio.com
Scientific contact	HI-Bio Clinical Program Lead, Hi-Bio, 1 408-548-7261, clinicaltrialdisclosure@hibio.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	02 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of MOR202 treatment in participants with anti-PLA2R antibody positive membranous nephropathy (aMN)

Protection of trial subjects:

This study was designed and conducted according to the ICH Harmonised Tripartite Guideline for Good Clinical Practices (GCP) and according to the Declaration of Helsinki that was in place during the time the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 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	Poland: 3
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	31
EEA total number of subjects	21

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)	24
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 65 participants were screened for this study. 31 participants were enrolled and received at least one dose of study drug.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (newly diagnosed or relapsed participants)

Arm description:

Participants with newly diagnosed or relapsed membranous nephropathy

Arm type	Experimental
Investigational medicinal product name	MOR202
Investigational medicinal product code	
Other name	felzartamab
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received MOR202 as an intravenous infusion over 6 treatment cycles of 28-days each. Dosing occurred weekly in Cycle 1 and every 4 weeks in Cycles 2 to 6.

Arm title	Cohort 2 (refractory participants)

Arm description:

Participants with membranous nephropathy refractory to immunosuppressive treatment

Arm type	Experimental
Investigational medicinal product name	MOR202
Investigational medicinal product code	
Other name	felzartamab
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received MOR202 as an intravenous infusion over 6 treatment cycles of 28-days each. Dosing occurred weekly in Cycle 1 and every 4 weeks in Cycles 2 to 6.

Number of subjects in period 1	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)
Started	18	13
Received at least one dose of study drug	18	13

Completed	13	10
Not completed	5	3
Physician decision	3	-
Use of prohibited therapy	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (newly diagnosed or relapsed participants)
Reporting group description:	
Participants with newly diagnosed or relapsed membranous nephropathy	
Reporting group title	Cohort 2 (refractory participants)
Reporting group description:	
Participants with membranous nephropathy refractory to immunosuppressive treatment	

Reporting group values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)	Total
Number of subjects	18	13	31
Age categorical			
The Full Analysis Set (FAS) included all participants who received at least one dose of study drug.			
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)	12	12	24
From 65-84 years	6	1	7
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	59.2	55.0	
standard deviation	± 11.34	± 12.47	-
Gender categorical			
Units: Subjects			
Female	5	2	7
Male	13	11	24
Race			
Units: Subjects			
White	13	8	21
Asian	4	0	4
Other	0	4	4
American Indian or Alaska Native	1	0	1
Black or African American	0	1	1

End points

End points reporting groups

Reporting group title	Cohort 1 (newly diagnosed or relapsed participants)
Reporting group description:	
Participants with newly diagnosed or relapsed membranous nephropathy	
Reporting group title	Cohort 2 (refractory participants)
Reporting group description:	
Participants with membranous nephropathy refractory to immunosuppressive treatment	

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events[1]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. SAEs were defined as death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized participant and required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section.

The Safety Analysis Set included all participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to week 25

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 summary statistics were planned for this endpoint.

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: participants	15	12		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events[2]

End point description:

An AE was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. SAEs were defined as death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized participant and

required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section.

The Safety Analysis Set included all participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to week 25

Notes:

[2] - 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 summary statistics were planned for this endpoint.

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: percentage of participants				
number (not applicable)	83.3	92.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Immunological Response Rate (BIRR)

End point title	Best Immunological Response Rate (BIRR)

End point description:

The best immunological response rate (BIRR) was defined as the percentage of participants with a best immunological response of stringent immunological complete response (sICR), immunological complete response (ICR), or immunological partial response (IPR) prior to the start of prohibited treatment or progression, based on reduction of serum anti-PLA2R antibody titre.

The FAS included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: percentage of participants				
number (confidence interval 95%)	83.3 (58.6 to 96.4)	61.5 (31.6 to 86.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Tested Positive for Anti-felzartamab Antibodies

End point title	Percentage of Participants Tested Positive for Anti-felzartamab Antibodies
End point description:	
The IAS included all participants with at least one antidrug antibody (ADA) result available.	
End point type	Secondary
End point timeframe:	
Up to 52 weeks	

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: percentage of participants				
number (not applicable)				
Baseline	6.7	7.7		
Post First Dose	6.7	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Titres of Participants Tested Positive for Anti-felzartamab Antibodies

End point title	Antibody Titres of Participants Tested Positive for Anti-felzartamab Antibodies
End point description:	
The IAS included all participants with at least one ADA result available. Here, the number of subjects analyzed = the number of participants with positive ADA titers. 99999 = data not available (N/A).	
End point type	Secondary
End point timeframe:	
Up to 52 weeks	

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: anti-felzartamab antibody titres				
arithmetic mean (standard deviation)				
Baseline (n=1,1)	13.10 (± 99999)	11.50 (± 99999)		
Post First Dose (n=1,0)	3.48 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Tested Positive for Anti-felzartamab Antibodies

End point title	Number of Participants Tested Positive for Anti-felzartamab Antibodies

End point description:

The Immunogenicity Analysis Set (IAS) included all participants with at least one antidrug antibody (ADA) result available.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: participants				
Baseline	1	1		
Post First Dose	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Felzartamab Serum Concentrations After Multiple Intravenous Administrations

End point title	Felzartamab Serum Concentrations After Multiple Intravenous Administrations

End point description:

The Pharmacokinetic Analysis Set (PKAS) included all participants with evaluable felzartamab serum concentration data. Here, "Subjects Analysed" is the number of participants evaluable for this outcome measure, and the row title shows the number of participants evaluated at each time point. 99999 = data not available (N/A).

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[3]	13[4]		
Units: nanogram(s)/millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
Pre-dose Cycle 1 Day 1 (C1D1) (n=18,13)	0.0 (± 0.0)	0.0 (± 0.0)		
Post-dose C1D1 (n=18,13)	323499.3 (± 98.3)	301417.5 (± 151.9)		
Pre-dose C1D8 (n=17,11)	89381.7 (± 97.9)	129924.9 (± 100.7)		
Post-dose C1D8 (n=17,11)	425669.4 (± 50.7)	429629.4 (± 91.7)		
Pre-dose C1D15 (n=17,12)	174658.7 (± 75.5)	189047.7 (± 80.9)		
Post-dose C1D15 (n=16,12)	456390.9 (± 70.6)	547940.5 (± 60.2)		
Pre-dose C1D22 (n=17,11)	185140.7 (± 78.0)	286607.9 (± 25.7)		
Post-dose C1D22 (n=17,10)	495612.5 (± 57.3)	656862.8 (± 29.7)		
Pre-dose C2D1 (n=17,12)	242903.4 (± 47.3)	148097.2 (± 193.7)		
Post-dose C2D1 (n=16,11)	474157.9 (± 108.0)	415814.9 (± 106.3)		
Pre-dose C3D1 (n=17,12)	34111.0 (± 164.7)	25879.8 (± 572.2)		
Pre-dose C4D1 (n=13,11)	19811.2 (± 218.1)	30655.9 (± 128.9)		
Pre-dose C5D1 (n=14,9)	27021.6 (± 152.0)	35176.1 (± 84.1)		
Pre-dose C6D1 (n=14,8)	28734.6 (± 116.9)	30383.0 (± 88.8)		
End of Treatment (n=17,10)	12367.0 (± 349.9)	33813.6 (± 61.9)		
Follow-up visit (n=1,0)	369.0 (± 99999)	99999 (± 99999)		
End of Study (n=1,0)	278.0 (± 99999)	99999 (± 99999)		

Notes:

[3] - Geometric mean was not calculable when n=0.
%CV was not calculable when n=0 or n=1.
[4] - Geometric mean was not calculable when n=0.
%CV was not calculable when n=0 or n=1.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with AEs During the Follow-up Period

End point title	Percentage of Participants with AEs During the Follow-up Period

End point description:

An AE was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. SAEs were defined as death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized participant and required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section.

The Safety Analysis Set included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Weeks 25 to 52

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: Percentage of participants				
number (not applicable)	44.4	38.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with AEs During the Follow-up Period

End point title	Number of Participants with AEs During the Follow-up Period

End point description:

An AE was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. SAEs were defined as death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized participant and required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section.

The Safety Analysis Set included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:
Weeks 25 to 52

End point values	Cohort 1 (newly diagnosed or relapsed participants)	Cohort 2 (refractory participants)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: participants	8	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 52 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0
Reporting groups	
Reporting group title	Cohort 1 Treatment Period
Reporting group description: Participants with newly diagnosed or relapsed membranous nephropathy	
Reporting group title	Cohort 2 Post Treatment
Reporting group description: -	
Reporting group title	Cohort 1 Post Treatment
Reporting group description: -	
Reporting group title	Cohort 2 Treatment Period
Reporting group description: Participants with membranous nephropathy refractory to immunosuppressive treatment	

Serious adverse events	Cohort 1 Treatment Period	Cohort 2 Post Treatment	Cohort 1 Post Treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)	1 / 13 (7.69%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (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
Infusion related reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (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
Nervous system disorders			
Cerebrovascular accident			

subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (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
Immune system disorders			
Type I hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (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			
COVID-19			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (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
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (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 Treatment Period		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 13 (23.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Type I hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1 Treatment Period	Cohort 2 Post Treatment	Cohort 1 Post Treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 18 (83.33%)	5 / 13 (38.46%)	8 / 18 (44.44%)

Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Venous thrombosis limb			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 18 (11.11%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Chest pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Fatigue			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	7	0	0
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Infusion site phlebitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vaccination site pain			

subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Generalised oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	7 / 18 (38.89%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	9	0	1
Drug hypersensitivity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Immunisation reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Pruritus genital			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Dysphonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Confusional state			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Euphoric mood			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Investigations			
Lipase increased			
subjects affected / exposed	3 / 18 (16.67%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	5	0	1
Lymphocyte percentage decreased			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood immunoglobulin G decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haematocrit decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Monocyte count increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			

Infusion related reaction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Animal bite			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eye contusion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 18 (16.67%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Carotid artery stenosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lethargy			

subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Anaemia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 13 (7.69%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Leukocytosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lymphocytosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			

subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	4 / 18 (22.22%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	13	0	0
Dry mouth			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pancreatitis acute			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Renal impairment			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nephrotic syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 18 (16.67%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	5	0	1

Back pain			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	4	0	0
Myalgia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	4	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Joint stiffness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	2
Conjunctivitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal bacterial infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Hyperkalaemia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Hypoferritinaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 13 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Iron deficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 18 (0.00%)	1 / 13 (7.69%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Steroid diabetes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 13 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 2 Treatment Period		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	12 / 13 (92.31%)		
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Venous thrombosis limb			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	7		
Chest pain			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	4		
Fatigue			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Infusion site phlebitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

Vaccination site pain subjects affected / exposed occurrences (all) Generalised oedema subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0 0 / 13 (0.00%) 0		
Immune system disorders Hypogammaglobulinaemia subjects affected / exposed occurrences (all) Drug hypersensitivity subjects affected / exposed occurrences (all) Immunisation reaction subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0		
Reproductive system and breast disorders Pruritus genital subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2 1 / 13 (7.69%) 2 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0		
Psychiatric disorders Insomnia			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Euphoric mood			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Investigations			
Lipase increased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Haematocrit decreased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Monocyte count increased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Neutrophil count increased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) Animal bite subjects affected / exposed occurrences (all) Eye contusion subjects affected / exposed occurrences (all) Skin laceration subjects affected / exposed occurrences (all)	 8 / 13 (61.54%) 8 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0		
Cardiac disorders Atrioventricular block first degree subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Carotid artery stenosis subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Hyperaesthesia	 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		

subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Lymphocytosis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Increased tendency to bruise			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Vertigo positional			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Eructation			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastrointestinal pain			

subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Pancreatitis acute subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 1 / 13 (7.69%) 2 0 / 13 (0.00%) 0		
Hepatobiliary disorders Bile duct stone subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) Renal impairment subjects affected / exposed occurrences (all) Nephrotic syndrome subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Arthralgia				
subjects affected / exposed	0 / 13 (0.00%)			
occurrences (all)	0			
Back pain				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences (all)	2			
Myalgia				
subjects affected / exposed	0 / 13 (0.00%)			
occurrences (all)	0			
Rhabdomyolysis				
subjects affected / exposed	2 / 13 (15.38%)			
occurrences (all)	2			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 13 (0.00%)			
occurrences (all)	0			
Joint stiffness				
subjects affected / exposed	0 / 13 (0.00%)			
occurrences (all)	0			
Infections and infestations				
Bronchitis				
subjects affected / exposed	4 / 13 (30.77%)			
occurrences (all)	4			
COVID-19				
subjects affected / exposed	2 / 13 (15.38%)			
occurrences (all)	2			
Conjunctivitis				
subjects affected / exposed	0 / 13 (0.00%)			
occurrences (all)	0			
Gastrointestinal bacterial infection				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	0 / 13 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				

subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypoferritinaemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Steroid diabetes			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 October 2019	Updated inclusion/exclusion criteria; additional minor changes
01 July 2020	Inclusion and exclusion criteria were updated; planned total number of clinical trial sites and locations updated; other minor updates

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported