Clinical trial results:
A Randomized, Double-Blind, Placebo Controlled Trial, Examining the Safety, Tolerability, Pharmacodynamic Effects and Pharmacokinetics of Temelimab Following Rituximab Treatment in Patients with Relapsing Forms of Multiple Sclerosis (RMS)

Summary

EudraCT number	2019-004822-15
Trial protocol	SE
Global end of trial date	24 January 2022

Results information

Result version number	v1 (current)
This version publication date	04 March 2023
First version publication date	04 March 2023

Trial information

Trial identification

Sponsor protocol code	GNC-401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04480307
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GeNeuro Innovation SAS
Sponsor organisation address	60A Avenue Rockfeller , Lyon, France, 69008
Public contact	Clinical Trials Information, GeNeuro Innovation SAS, +41 22552 4800, contact@geneuro.com
Scientific contact	Clinical Trials Information, GeNeuro Innovation SAS, +41 22552 4800, contact@geneuro.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	24 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 January 2022
Global end of trial reached?	Yes
Global end of trial date	24 January 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 temelimab following intravenous (IV) administration of 18 mg/kg, 36 mg/kg or 54 mg/kg, in patients with RMS who have been treated with rituximab for at least 1 year

Protection of trial subjects:

All patients were to be observed for 6 hours following completion of the first IMP infusion and at least 2 hours following completion of the subsequent IMP infusions (2nd to 12th).
At Week 48 (and/or Week 46 for the various PD/PK measurements, clinical efficacy, MRI, PD, PK and QoL assessments were performed for comparison with the assessments at Baseline. Safety assessments were carried out at all visits.
In case of premature discontinuation of the Investigational Medicinal Product (IMP), the patient was withdrawn from the study. Reasons for premature discontinuation of the IMP were: Adverse Events or conditions which, according to the judgement of the investigator, constituted a hazard to the patient if the treatment with the IMP continued, including lack of efficacy; major protocol deviations if they interfered to an unacceptable extent with study procedures or assessments, or if they jeopardised patient's safety, or administration of an unauthorised concomitant treatment, patient becoming pregnant, participation in any other interventional clinical trial.

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	23 June 2020
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	Sweden: 41
Worldwide total number of subjects	41
EEA total number of subjects	41

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	41
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who met the inclusion criteria at the Screening visit (within 3 weeks prior to dosing) and at the Baseline visit (Study Day 1 [SD1]) were considered eligible to participate in the clinical study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Temelimab 18 mg/kg

Arm description:

Temelimab 18 mg/kg given by IV infusion every 4 weeks for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Temelimab
Investigational medicinal product code	GNbAC1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Temelimab was administered by IV infusion (200 mL over 2 hours) following dilution into glucose 5% solution

Arm title	Temelimab 36 mg/kg

Arm description:

Temelimab 36 mg/kg given by IV infusion every 4 weeks for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Temelimab
Investigational medicinal product code	GNbAC1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Temelimab was administered by IV infusion (200 mL over 2 hours) following dilution into glucose 5% solution

Arm title	Temelimab 54 mg/kg

Arm description:

Temelimab 54 mg/kg given by IV infusion every 4 weeks for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Temelimab
Investigational medicinal product code	GNbAC1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Temelimab was administered by IV infusion (200 mL over 2 hours) following dilution into glucose 5% solution

Arm title	Placebo

Arm description:

Placebo given by IV infusion every 4 weeks for 48 weeks

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

Dosage and administration details:

Placebo was administered by IV infusion (200 mL over 2 hours) following dilution into glucose 5% solution

Number of subjects in period 1	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg
Started	11	10	10
Completed	11	9	10
Not completed	0	1	0
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	Placebo
Started	10
Completed	9
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Temelimab 18 mg/kg
Reporting group description:	
Temelimab 18 mg/kg given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 36 mg/kg
Reporting group description:	
Temelimab 36 mg/kg given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 54 mg/kg
Reporting group description:	
Temelimab 54 mg/kg given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo given by IV infusion every 4 weeks for 48 weeks	

Reporting group values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg
Number of subjects	11	10	10
Age categorical			
Adults (18-64 years)			
Units: Subjects			
Adults (18-64 years)	11	10	10
Age continuous			
Units: years			
arithmetic mean	43.2	47.9	45.2
standard deviation	± 7.3	± 6.3	± 10.2
Gender categorical			
Units: Subjects			
Female	7	5	3
Male	4	5	7

Reporting group values	Placebo	Total	
Number of subjects	10	41	
Age categorical			
Adults (18-64 years)			
Units: Subjects			
Adults (18-64 years)	10	41	
Age continuous			
Units: years			
arithmetic mean	45.6		
standard deviation	± 9.4	-	
Gender categorical			
Units: Subjects			
Female	6	21	
Male	4	20	

Subject analysis sets

Subject analysis set title	Randomised set (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients to whom a therapeutic treatment was randomly assigned using an interactive response system. Patients were analysed in their randomisation group whatever the treatment they received

Subject analysis set title	Safety set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients having taken at least one dose of IMP. Patients were allocated to the group based on the treatment they received.

Subject analysis set title	Per protocol set (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

All patients of the RS with no major protocol deviations and with at least 9 infusions performed. All protocol deviations were assessed and documented on a case-by-case basis prior to database lock, and deviations considered to have a serious impact on the efficacy results led to the relevant patient being excluded from the set.

Reporting group values	Randomised set (RS)	Safety set (SAF)	Per protocol set (PP)
Number of subjects	41	41	35
Age categorical			
Adults (18-64 years)			
Units: Subjects			
Adults (18-64 years)	41	41	35
Age continuous			
Units: years			
arithmetic mean	45.4	45.4	30.2
standard deviation	± 8.3	± 8.3	± 6.0
Gender categorical			
Units: Subjects			
Female	21	21	18
Male	20	20	17

End points

End points reporting groups

Reporting group title	Temelimab 18 mg/kg
Reporting group description:	
Temelimab 18 mg/kg given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 36 mg/kg
Reporting group description:	
Temelimab 36 mg/kg given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 54 mg/kg
Reporting group description:	
Temelimab 54 mg/kg given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo given by IV infusion every 4 weeks for 48 weeks	
Subject analysis set title	Randomised set (RS)
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients to whom a therapeutic treatment was randomly assigned using an interactive response system. Patients were analysed in their randomisation group whatever the treatment they received	
Subject analysis set title	Safety set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients having taken at least one dose of IMP. Patients were allocated to the group based on the treatment they received.	
Subject analysis set title	Per protocol set (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients of the RS with no major protocol deviations and with at least 9 infusions performed. All protocol deviations were assessed and documented on a case-by-case basis prior to database lock, and deviations considered to have a serious impact on the efficacy results led to the relevant patient being excluded from the set.	

Primary: Safety and tolerability

End point title	Safety and tolerability[1]
End point description:	
Analysis of AEs focused on TEAEs, defined as AEs	
End point type	Primary
End point timeframe:	
From the time the patient received their first dose of IMP until their last study visit +28 days.	

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: Statistics were provided depending on the nature of considered data.
This was a Phase IIa study, the primary objective being the safety.
No statistical analysis was planned in the SAP for safety endpoints. Numbers and types of Adverse Events were simply described and compared across arms.

End point values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: number				
number (not applicable)				
TEAEs	10	9	10	9

End point values	Safety set (SAF)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: number				
number (not applicable)				
TEAEs	38			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in MTSat in cortex

End point title	Change in MTSat in cortex

End point description:

Change in magnetisation transfer saturation (MTSat) in cortex at Week 48 compared to Baseline

End point type	Secondary

End point timeframe:

From Baselise at week 48

End point values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	6	7
Units: number				
arithmetic mean (standard deviation)	0.037 (± 0.058)	0.044 (± 0.044)	-0.013 (± 0.077)	0.018 (± 0.040)

End point values	Per protocol set (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: number				
arithmetic mean (standard deviation)	0.027 (± 0.061)			

Statistical analyses

Statistical analysis title	ANCOVA analysis
Statistical analysis description:	
Change in MTSat in Cortex from Baseline at Week 48 was analysed using a parametric analysis of covariance (ANCOVA) including Baseline and treatment as factor	
Comparison groups	Temelimab 18 mg/kg v Temelimab 36 mg/kg v Temelimab 54 mg/kg
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9472
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.052
upper limit	0.049

Statistical analysis title	Bayesian analyses
Statistical analysis description:	
In addition, exploratory Bayesian analysis was done using a non-informative prior on the mean observed difference.	
Comparison groups	Temelimab 18 mg/kg v Temelimab 36 mg/kg v Temelimab 54 mg/kg
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference of change from Baseline
Point estimate	0.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.036
upper limit	0.059

Secondary: Change in T1 lesion volume

End point title	Change in T1 lesion volume

End point description: Change in T1 lesion volume at Week 48 compared to Baseline	
End point type	Secondary
End point timeframe: From Baseline at week 48	

End point values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	9	8
Units: number				
arithmetic mean (standard deviation)	-0.055 (± 0.315)	-0.032 (± 0.686)	0.227 (± 0.405)	-0.044 (± 0.185)

End point values	Per protocol set (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: number				
arithmetic mean (standard deviation)	0.047 (± 0.493)			

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Temelimab 36 mg/kg v Temelimab 54 mg/kg v Temelimab 18 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4027
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.154
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.216
upper limit	0.524

Secondary: Change in T2 lesion volume

End point title	Change in T2 lesion volume

End point description: Change in T2 lesion volume at Week 48 compared to Baseline	
End point type	Secondary
End point timeframe: From Baseline at Week 48	

End point values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	9	8
Units: number				
arithmetic mean (standard deviation)	0.028 (± 0.085)	0.029 (± 0.088)	0.023 (± 0.061)	0.027 (± 0.075)

End point values	Per protocol set (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: number				
arithmetic mean (standard deviation)	0.027 (± 0.076)			

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Temelimab 18 mg/kg v Temelimab 36 mg/kg v Temelimab 54 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7428
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.051
upper limit	0.071

Secondary: Change in brain parenchymal volume fraction

End point title	Change in brain parenchymal volume fraction

End point description: Change in brain parenchymal volume fraction at Week 48 compared to Baseline	
End point type	Secondary
End point timeframe: From baseline at Week 48	

End point values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	9	8
Units: number				
arithmetic mean (standard deviation)	-0.013 (± 0.011)	-0.021 (± 0.032)	-0.011 (± 0.013)	-0.019 (± 0.017)

End point values	Per protocol set (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: number				
arithmetic mean (standard deviation)	-0.015 (± 0.021)			

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Temelimab 36 mg/kg v Temelimab 18 mg/kg v Temelimab 54 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7314
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.013
upper limit	0.018

Secondary: Change in thalamic volume fraction

End point title	Change in thalamic volume fraction

End point description: Change in thalamic volume fraction at Week 48 compared to Baseline	
End point type	Secondary
End point timeframe: From baseline at Week 48	

End point values	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	9	8
Units: number				
arithmetic mean (standard deviation)	-0.000 (± 0.000)	-0.000 (± 0.000)	-0.000 (± 0.000)	-0.000 (± 0.000)

End point values	Per protocol set (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: number				
arithmetic mean (standard deviation)	-0.000 (± 0.000)			

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Temelimab 18 mg/kg v Temelimab 36 mg/kg v Temelimab 54 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7662
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Analysis of AEs focused on TEAEs, defined as AEs that occurred from the time the patient sign the informed consent onwards until the patient's last study visit +28 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Temelimab 18 mg/mL

Reporting group description:

Temelimab 18 mg/mL given by IV infusion every 4 weeks for 48 weeks

Reporting group title	Temelimab 36 mg/mL

Reporting group description:

Temelimab 36 mg/mL given by IV infusion every 4 weeks for 48 weeks

Reporting group title	Temelimab 54 mg/mL

Reporting group description:

Temelimab 54 mg/mL given by IV infusion every 4 weeks for 48 weeks

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Temelimab 18 mg/mL	Temelimab 36 mg/mL	Temelimab 54 mg/mL
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (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
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2.5 %

Non-serious adverse events	Temelimab 18 mg/mL	Temelimab 36 mg/mL	Temelimab 54 mg/mL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	9 / 10 (90.00%)	10 / 10 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 11 (27.27%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	3	1	1
Fatigue			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Peripheral swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			

Vulvovaginal pruritus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Prostatic disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 11 (18.18%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
depression			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Sleep disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Fall			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Animal bite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			

subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Patella fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Balance disorder			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vertigo positional			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral mucosal exfoliation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 11 (27.27%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	3	2	1

Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	2 / 11 (18.18%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Arthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 11 (45.45%)	4 / 10 (40.00%)	5 / 10 (50.00%)
occurrences (all)	5	4	5
COVID-19			
subjects affected / exposed	3 / 11 (27.27%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Bacterial vaginosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lyme disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Norovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Periodontitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	2 / 11 (18.18%)	4 / 10 (40.00%)	0 / 10 (0.00%)
occurrences (all)	2	4	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Fatigue			

subjects affected / exposed occurrences (all) Peripheral swelling subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0		
Reproductive system and breast disorders Vulvovaginal pruritus subjects affected / exposed occurrences (all) Prostatic disorder subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0		
Psychiatric disorders depression subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0		
Investigations Blood pressure increased subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0		
Injury, poisoning and procedural complications			

Post lumbar puncture syndrome subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Fall subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Animal bite subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Ligament sprain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Patella fracture subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Tooth fracture subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Balance disorder subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Paraesthesia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Dizziness				

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) Vertigo positional subjects affected / exposed occurrences (all)	 2 / 10 (20.00%) 2 0 / 10 (0.00%) 0		
Gastrointestinal disorders Stomatitis subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Oral mucosal exfoliation subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Dermatitis allergic	 1 / 10 (10.00%) 1 		

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Bursitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Limb discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tendonitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
COVID-19			

subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Bacterial vaginosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lyme disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Norovirus infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Periodontitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported