Clinical trial results:
A long-term extension of Study GNC-401 with temelimab in patients with Relapsing forms of Multiple Sclerosis (RMS) under treatment with rituximab

Summary

EudraCT number	2021-001973-21
Trial protocol	SE
Global end of trial date	30 April 2022

Results information

Result version number	v1 (current)
This version publication date	17 June 2023
First version publication date	17 June 2023

Trial information

Trial identification

Sponsor protocol code	GNC-402

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05049161
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	30 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2022
Global end of trial reached?	Yes
Global end of trial date	30 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the long-term 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 are treated with rituximab for at least 1 year and who participated to the clinical study GNC-401. Patients who had been on placebo in study GNC-401 were randomised to temelimab, see below for details in "Subject disposition, Recruitment".

Protection of trial subjects:

All patients were to be observed for 2 hours following completion of the first three IMP infusions and for at least 1 hour following completion of the subsequent IMP infusions. Intra patient dose escalation of temelimab was not permitted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	33
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients randomised to placebo in study GNC-401 were rerandomised to temelimab 18 mg/kg, 36 mg/kg or 54 mg/kg (1:1:1) on D1 of study GNC-402 using a web based IRS with predefined randomisation list with blocks. Patients who received temelimab in study GNC 401 continued with the same dose in study GNC-402 without the need for re-randomisation.

Pre-assignment

Screening details:

Patients who met all the inclusion criteria were eligible for inclusion in the 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

Blinding implementation details:

The present study GNC-402, was performed in double-blind fashion in patients who had completed study GNC-401. At entry, all patients received active treatment with temelimab. On D1 (Baseline, Visit 1 [V1]), the patients of the placebo group in study GNC-401 were re-randomised to temelimab 18 mg/kg, 36 mg/kg or 54 mg/kg (1:1:1), while the patients who received temelimab in study GNC-401 continued with the same dose.

Arms

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

Arm description:

Temelimab 18 mg/kg was planned to be 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 was planned to be 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 was planned to be 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

Number of subjects in period 1	Temelimab 18 mg/kg	Temelimab 36 mg/kg	Temelimab 54 mg/kg
Started	13	11	9
Completed	13	11	9

Baseline characteristics

Reporting groups	
Reporting group title	Temelimab 18 mg/kg
Reporting group description:	
Temelimab 18 mg/kg was planned to be given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 36 mg/kg
Reporting group description:	
Temelimab 36 mg/kg was planned to be given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 54 mg/kg
Reporting group description:	
Temelimab 54 mg/kg was planned to be 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	13	11	9
Age categorical Units: Subjects			
Adults (18-64 years)			
Age continuous Units: years			
arithmetic mean	44.8	44.1	49.1
standard deviation	± 7.3	± 9.4	± 4.8
Gender categorical Units: Subjects			
Female	9	5	4
Male	4	6	5

Reporting group values	Total		
Number of subjects	33		
Age categorical Units: Subjects			
Adults (18-64 years)	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	18		
Male	15		

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 a web-based interactive response system. Patients were analysed in their randomisation group whatever treatment they

received.

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

Reporting group values	Randomised set (RS)	Safety set (SAF)	
Number of subjects	33	33	
Age categorical Units: Subjects			
Adults (18-64 years)			
Age continuous Units: years			
arithmetic mean	45.7	45.7	
standard deviation	± 7.6	± 7.6	
Gender categorical Units: Subjects			
Female	18	18	
Male	15	15	

End points

End points reporting groups

Reporting group title	Temelimab 18 mg/kg
Reporting group description:	
Temelimab 18 mg/kg was planned to be given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 36 mg/kg
Reporting group description:	
Temelimab 36 mg/kg was planned to be given by IV infusion every 4 weeks for 48 weeks	
Reporting group title	Temelimab 54 mg/kg
Reporting group description:	
Temelimab 54 mg/kg was planned to be 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 a web-based interactive response system. Patients were analysed in their randomisation group whatever treatment they received.	
Subject analysis set title	Safety set (SAF)
Subject analysis set type	Full 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.	

Primary: Safety and Tolerability

End point title	Safety and Tolerability[1]
End point description:	
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	Safety set (SAF)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	13	11	9	33
Units: TEAEs	7	9	7	23

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time the patient received his/her first dose of IMP until his/her last study visit +28 days

Adverse event reporting additional description:

When an AE occurred after written consent had been obtained but before the first dose of study treatment, the AE was considered a non-treatment emergent AE (also termed 'pre treatment AE').

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 was planned to be given as monthly (4-weekly) IV infusions for 48 weeks (12 administrations in total).

Reporting group title	Temelimab 36 mg/mL

Reporting group description:

Temelimab 36 mg/mL was planned to be given as monthly (4-weekly) IV infusions for 48 weeks (12 administrations in total).

Reporting group title	Temelimab 54 mg/mL

Reporting group description:

Temelimab 54 mg/mL was planned to be given as monthly (4-weekly) IV infusions for 48 weeks (12 administrations in total).

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	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 9 (11.11%)
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	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	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	7 / 13 (53.85%)	9 / 11 (81.82%)	7 / 9 (77.78%)
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Meralgia paraesthetica			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Fatigue			

subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 13 (15.38%)	2 / 11 (18.18%)	4 / 9 (44.44%)
occurrences (all)	1	1	1
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 11 (27.27%)	3 / 9 (33.33%)
occurrences (all)	1	1	1
Sinusitis			

subjects affected / exposed	2 / 13 (15.38%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

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? Yes

Date	Interruption	Restart date
30 April 2022	All patients were withdrawn from the study prematurely when the Sponsor decided to stop the study since temelimab was not available for clinical supply, following the worldwide shortage of culture media and supplementary reagents due to COVID-19 pandemic. The overall mean (SD) study duration was 15.0 weeks (7.6), which was similar between treatment groups. At time of termination, 33 patients were still receiving treatment with temelimab in study GNC-402 in Sweden.	-

Notes:

Limitations and caveats

None reported