Clinical trial results:
A randomized, open-label, two arm, parallel group, proof-of-concept clinical trial to investigate the efficacy and safety of LNP023 compared with rituximab in the treatment of subjects with idiopathic membranous nephropathy

Summary

EudraCT number	2019-001734-34
Trial protocol	GB CZ NL ES DE FR
Global end of trial date	20 January 2023

Results information

Result version number	v1 (current)
This version publication date	28 January 2024
First version publication date	28 January 2024

Trial information

Trial identification

Sponsor protocol code	CLNP023D12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04154787
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of LNP023 compared with rituximab.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	China: 3
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	India: 7
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Taiwan: 1
Worldwide total number of subjects	37
EEA total number of subjects	16

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)	34
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 18 investigative sites in 9 countries/regions: Argentina (3), Czech Republic (1), Germany (4), India (2), Netherlands (1), Spain (2), United Kingdom (3), China (1) and Taiwan (1)

Pre-assignment

Screening details:

Overall, 37 (100%) subjects were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LNP023 10/50 mg b.i.d.

Arm description:

As per protocol V00, participants took LNP023 10 mg orally b.i.d. for 4 weeks followed by LNP023 50 mg orally b.i.d. for 20 weeks

Arm type	Experimental
Investigational medicinal product name	Iptacopan
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LNP023 10/50 mg b.i.d.

Arm title	LNP023 200 mg b.i.d.

Arm description:

Combination of the LNP023 25/200 mg b.i.d. and 50/200 mg b.i.d. groups. Under protocol V00, participants took LNP023 25 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks. Under protocol v01, participants took LNP023 50 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks.

Arm type	Experimental
Investigational medicinal product name	Iptacopan
Investigational medicinal product code	LNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LNP023 25/200 mg b.i.d. and 50/200 mg b.i.d.

Arm title	Rituximab

Arm description:

Rituximab 1 g i.v. at Day 1 and Day 15

Arm type	Active comparator

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 1 g i.v. at Day 1 and Day 15

Number of subjects in period 1	LNP023 10/50 mg b.i.d.	LNP023 200 mg b.i.d.	Rituximab
Started	3	19	15
Completed	3	9	14
Not completed	0	10	1
Patient Requires Other Treatment	-	1	-
Subject Decision	-	1	-
Adverse event, non-fatal	-	1	-
Study Terminated By Sponsor	-	6	1
Suspected Lack Of Efficacy	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	LNP023 10/50 mg b.i.d.
Reporting group description:	
As per protocol V00, participants took LNP023 10 mg orally b.i.d. for 4 weeks followed by LNP023 50 mg orally b.i.d. for 20 weeks	
Reporting group title	LNP023 200 mg b.i.d.
Reporting group description:	
Combination of the LNP023 25/200 mg b.i.d. and 50/200 mg b.i.d. groups. Under protocol V00, participants took LNP023 25 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks. Under protocol v01, participants took LNP023 50 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks.	
Reporting group title	Rituximab
Reporting group description:	
Rituximab 1 g i.v. at Day 1 and Day 15	

Reporting group values	LNP023 10/50 mg b.i.d.	LNP023 200 mg b.i.d.	Rituximab
Number of subjects	3	19	15
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	19	13
From 65-84 years	1	0	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	55.0	48.9	46.7
standard deviation	± 18.52	± 8.84	± 15.33
Sex: Female, Male Units: participants			
Female	1	4	1
Male	2	15	14
Race/Ethnicity, Customized Units: Subjects			
Asian	1	5	4
Black Or African American	0	0	1
Unknown	0	0	1
White	2	14	9

Reporting group values	Total		
Number of subjects	37		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	34		
From 65-84 years	3		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	6		
Male	31		
Race/Ethnicity, Customized Units: Subjects			
Asian	10		
Black Or African American	1		
Unknown	1		
White	25		

End points

End points reporting groups

Reporting group title	LNP023 10/50 mg b.i.d.

Reporting group description:

As per protocol V00, participants took LNP023 10 mg orally b.i.d. for 4 weeks followed by LNP023 50 mg orally b.i.d. for 20 weeks

Reporting group title	LNP023 200 mg b.i.d.

Reporting group description:

Combination of the LNP023 25/200 mg b.i.d. and 50/200 mg b.i.d. groups. Under protocol V00, participants took LNP023 25 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks. Under protocol v01, participants took LNP023 50 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks.

Reporting group title	Rituximab

Reporting group description:

Rituximab 1 g i.v. at Day 1 and Day 15

Subject analysis set title	LNP023 10 mg b.i.d.
Subject analysis set type	Per protocol

Subject analysis set description:

Low dose of LNP023 under Protocol V00, LNP023 10mg taken orally b.i.d. during the first 4 weeks of treatment. PK (pharmacokinetic) analysis set included all participants with at least one available valid PK concentration measurement.

Subject analysis set title	LNP023 50 mg b.i.d. (20-week administration)
Subject analysis set type	Per protocol

Subject analysis set description:

Under Protocol V00, LNP023 50mg taken orally b.i.d. during the last 20 weeks of treatment. PK (pharmacokinetic) analysis set included all participants with at least one available valid PK concentration measurement.

Subject analysis set title	LNP023 25 mg b.i.d.
Subject analysis set type	Per protocol

Subject analysis set description:

High dose of LNP023 under Protocol V00, LNP023 25mg taken orally b.i.d. during the first 4 weeks of treatment. PK (pharmacokinetic) analysis set included all participants with at least one available valid PK concentration measurement.

Subject analysis set title	LNP023 50 mg b.i.d. (4-week administration)
Subject analysis set type	Per protocol

Subject analysis set description:

Under Protocol V01, LNP023 50mg taken orally b.i.d. during the first 4 weeks of treatment. PK (pharmacokinetic) analysis set included all participants with at least one available valid PK concentration measurement.

Subject analysis set title	LNP023 200 mg b.i.d.
Subject analysis set type	Per protocol

Subject analysis set description:

Under protocol V00, participants took LNP023 25 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks.
Under protocol v01, participants took LNP023 50 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks.
PK (pharmacokinetic) analysis set included all participants with at least one available valid PK concentration measurement.

Primary: Ratio between baseline Urine Protein Creatinine Ratio (UPCR) and Urine Protein Creatinine Ratio at 24 weeks of treatment (from 24h urine collection)

End point title	Ratio between baseline Urine Protein Creatinine Ratio (UPCR) and Urine Protein Creatinine Ratio at 24 weeks of treatment (from 24h urine collection)[1]

End point description:

The primary endpoint of this study is the ratio between UPCR at 24 weeks of treatment measured in 24h urine and baseline UPCR .
To assess the primary objective, the log-transformed ratio to baseline in UPCR was analyzed using a mixed model for repeated measures (MMRM). The results were back transformed and presented on the original scale.

End point type	Primary

End point timeframe:

Baseline, Day 113, Day 169

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this primary outcome.

End point values	LNP023 200 mg b.i.d.	Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: ratio to baseline				
geometric mean (confidence interval 95%)				
Day 113 (n=10, 13)	0.94 (0.74 to 1.20)	0.89 (0.71 to 1.10)		
Day 169 (n=9, 9)	0.88 (0.65 to 1.19)	0.64 (0.48 to 0.86)		

Statistical analyses

Statistical analysis title	UPCR ratio
Comparison groups	Rituximab v LNP023 200 mg b.i.d.
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.267 [2]
Method	Mixed models analysis
Parameter estimate	Adjusted geometric mean ratio
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	2.08

Notes:

[2] - Calculated at one-sided 10% level from a lower-tailed test

Secondary: Change from baseline in plasma levels of circulating fragment of factor B (Bb)

End point title	Change from baseline in plasma levels of circulating fragment of factor B (Bb)[3]

End point description:

The drug (LNP023) is expected to block the complement alternative pathway dysregulation and thereby should normalize complement biomarker levels in serum. Bb is a biomarker that accurately reflects the level of complement Alternative Pathway activation.

Baseline is defined as the last non-missing measurement prior to randomization.
Measurements for LNP023 group were done pre-dose.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29, Day 57, Day 113 and Day 169

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	13		
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 15 (n=17, 13)	1520.59 (± 9370.086)	-417.69 (± 701.667)		
Day 29 (n=15, 13)	-732.00 (± 1412.633)	-318.46 (± 604.440)		
Day 57 (n=14, 13)	-545.00 (± 1379.201)	-75.38 (± 787.545)		
Day 113 (n=11, 12)	-877.27 (± 1562.716)	-219.17 (± 703.568)		
Day 169 (n=10, 9)	-984.00 (± 1794.419)	-570.00 (± 611.167)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in plasma levels of sC5b-9

End point title	Change from baseline in plasma levels of sC5b-9[4]

End point description:

Soluble C5b-9 (sC5b-9) is a biomarker of the complement pathway activity that correlate with disease progression.
Baseline is defined as the last non-missing measurement prior to randomization.
Measurements for LNP023 group were done pre-dose.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29, Day 57, Day 113, Day 169

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	13		
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 15 (n=17, 13)	-80.40 (± 98.229)	-38.49 (± 52.258)		

Day 29 (n=15, 13)	-82.80 (± 118.338)	-24.51 (± 94.826)		
Day 57 (n=14, 13)	-90.62 (± 108.483)	-14.02 (± 107.651)		
Day 113 (n=11, 12)	-113.32 (± 108.118)	-24.95 (± 128.721)		
Day 169 (n=10, 9)	-84.07 (± 96.045)	-21.76 (± 122.654)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to baseline of urine protein creatinine ratio (UPCR) measured in first morning void

End point title	Ratio to baseline of urine protein creatinine ratio (UPCR) measured in first morning void[5]

End point description:

Adjusted geometric mean ratio to baseline of Urine Protein Creatinine Ratio (UPCR) measured in first morning void.
First morning void urine sample was collected in the morning of the day before the visit and kept in the fridge.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29, Day 57, Day 85, Day 113, Day 141, Day 169, Day 266 and Day 378

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: ratio to baseline				
geometric mean (confidence interval 95%)				
Day 15 (n=15, 11)	0.94 (0.65 to 1.34)	1.15 (0.75 to 1.76)		
Day 29 (n=18, 12)	0.98 (0.70 to 1.36)	0.90 (0.60 to 1.35)		
Day 57 (n=14, 12)	1.02 (0.71 to 1.48)	0.77 (0.51 to 1.16)		
Day 85 (n=11, 13)	1.03 (0.68 to 1.56)	0.75 (0.50 to 1.13)		
Day 113 (n=10, 11)	1.05 (0.68 to 1.63)	0.92 (0.60 to 1.41)		
Day 141 (n=10, 9)	0.75 (0.48 to 1.19)	0.77 (0.48 to 1.23)		
Day 169 (n=9, 9)	0.72 (0.44 to 1.16)	0.55 (0.34 to 0.89)		
Day 266 (n=6, 7)	0.57 (0.33 to 0.99)	0.34 (0.20 to 0.57)		
Day 378 (End Of Study) (n=8, 8)	0.37 (0.22 to 0.63)	0.46 (0.27 to 0.76)		

Statistical analyses

Statistical analysis title	Ratio at Day 169
Statistical analysis description: Day 169	
Comparison groups	LNP023 200 mg b.i.d. v Rituximab
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4528 [6]
Method	Mixed Model for Repeated Measures
Parameter estimate	Geometric mean ratios
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.61

Notes:

[6] - Calculated from a two-sided test at the 0.05 significance level

Statistical analysis title	Ratio at Day 15
Statistical analysis description: Day 15	
Comparison groups	LNP023 200 mg b.i.d. v Rituximab
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4598 [7]
Method	Mixed Model for Repeated Measures
Parameter estimate	Adjusted geometric mean ratios
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.42

Notes:

[7] - Calculated from a two-sided test at the 0.05 significance level

Secondary: Proportion of participants by treatment response at 24 weeks of treatment

End point title	Proportion of participants by treatment response at 24 weeks of treatment[8]

End point description:

Participants were considered complete responders if at 24 weeks of treatment, they showed complete remission of proteinuria (i.e., Urine Protein (UP) ≤ 0.3 g/24h), partial responders if they showed partial remission (i.e., UP > 0.3g/24h and ≤ 3.5 g/24h and a reduction of UP by >50% from baseline), and non-responders if UP >3.5g/24h and/or reduction of UP from baseline <50%.

End point type	Secondary

End point timeframe:

Baseline, Day 169

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: participants				
Complete	0	0		
Partial	2	2		
No response	7	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in (eGFR) estimated Glomerular Filtration Rate over time

End point title	Change from baseline in (eGFR) estimated Glomerular Filtration Rate over time[9]

End point description:

Changes in renal function were assessed via estimated glomerular filtration rate (eGFR).
Change in eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29, Day 57, Day 85, Day 113, Day 141, Day 169

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	13		
Units: mL/min/1.73 m^2				
arithmetic mean (standard deviation)				
Day 15 (n=18, 13)	2.3 (± 12.07)	0.3 (± 8.33)		
Day 29 (n=19, 13)	-0.5 (± 8.53)	6.1 (± 10.44)		
Day 57 (n=14, 13)	2.0 (± 11.10)	9.2 (± 21.05)		
Day 85 (n=12, 13)	-1.6 (± 11.53)	10.2 (± 16.40)		

Day 113 (n=11, 11)	1.2 (± 8.64)	10.8 (± 15.41)		
Day 141 (n=10, 9)	-1.8 (± 9.10)	7.1 (± 9.29)		
Day 169 (n=10, 9)	-1.3 (± 7.36)	3.1 (± 13.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic parameter Cmax in plasma

End point title	Pharmacokinetic parameter Cmax in plasma[10]

End point description:

Pharmacokinetics of LNP023: Cmax is the maximum (peak) observed plasma drug concentration after dose administration (mass x volume-1)

End point type	Secondary

End point timeframe:

Day 29 and Day 113 (pre-dose and 0.25 hours, 0.5 hours, 1 hour 2 hours, 4 hours and 6 hours post dose)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	LNP023 10 mg b.i.d.	LNP023 50 mg b.i.d. (20-week administration)	LNP023 25 mg b.i.d.
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	2	2	3
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 0, 2, 3, 10, 0)	999 (± 999)	1200 (± 799)	999 (± 999)	2070 (± 938)
Day 113 (n= 7, 0, 0, 0, 2)	4810 (± 2850)	999 (± 999)	1220 (± 304)	999 (± 999)

End point values	LNP023 50 mg b.i.d. (4-week administration)			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 0, 2, 3, 10, 0)	2140 (± 917)			
Day 113 (n= 7, 0, 0, 0, 2)	999 (± 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic parameter Tmax in plasma

End point title	Pharmacokinetic parameter Tmax in plasma[11]

End point description:

Pharmacokinetics of LNP023 : Tmax is the time to reach maximum (peak) plasma drug concentration after dose administration (time).
Actual sampling time points were considered for the calculation of PK parameters.

End point type	Secondary

End point timeframe:

Day 29 and Day 113 (pre-dose and 0.25 hours, 0.5 hours, 1 hour 2 hours, 4 hours and 6 hours post dose)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	LNP023 10 mg b.i.d.	LNP023 50 mg b.i.d. (20-week administration)	LNP023 25 mg b.i.d.
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	2	2	3
Units: hours				
median (full range (min-max))				
Day 29 (n= 0, 2, 3, 10, 0)	999 (999 to 999)	2.04 (2.00 to 2.08)	999 (999 to 999)	2.00 (1.00 to 4.00)
Day 113 (n= 7, 0, 0, 0, 2)	1.00 (0.250 to 6.00)	999 (999 to 999)	2.05 (2.00 to 2.10)	999 (999 to 999)

End point values	LNP023 50 mg b.i.d. (4-week administration)			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hours				
median (full range (min-max))				
Day 29 (n= 0, 2, 3, 10, 0)	2.03 (1.00 to 4.38)			
Day 113 (n= 7, 0, 0, 0, 2)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic parameter AUClast in plasma

End point title	Pharmacokinetic parameter AUClast in plasma[12]

End point description:

Pharmacokinetics of LNP023: AUClast is the AUC from time zero to the last measurable concentration sampling time (tlast) (mass x time x volume-1)

End point type	Secondary

End point timeframe:

Day 29 and Day 113 (pre-dose and 0.25 hours, 0.5 hours, 1 hour 2 hours, 4 hours and 6 hours post dose)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	LNP023 10 mg b.i.d.	LNP023 50 mg b.i.d. (20-week administration)	LNP023 25 mg b.i.d.
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	2	2	3
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 0, 2, 3, 10, 0)	999 (± 999)	5970 (± 4150)	999 (± 999)	8140 (± 3080)
Day 113 (n= 7, 0, 0, 0, 2)	22200 (± 15600)	999 (± 999)	5940 (± 989)	999 (± 999)

End point values	LNP023 50 mg b.i.d. (4-week administration)			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 0, 2, 3, 10, 0)	9920 (± 3960)			
Day 113 (n= 7, 0, 0, 0, 2)	999 (± 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic parameter AUCtau in plasma

End point title	Pharmacokinetic parameter AUCtau in plasma[13]

End point description:

Pharmacokinetics of LNP023 : AUCtau is the AUC calculated to the end of a dosing interval (tau) at steady-state (amount x time x volume-1)

End point type	Secondary

End point timeframe:

Day 29 and Day 113 (pre-dose and 0.25 hours, 0.5 hours, 1 hour 2 hours, 4 hours and 6 hours post dose)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.	LNP023 10 mg b.i.d.	LNP023 50 mg b.i.d. (20-week administration)	LNP023 25 mg b.i.d.
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	2	2	3
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 0, 2, 3, 10, 0)	999 (± 999)	9850 (± 5790)	999 (± 999)	12800 (± 3490)
Day 113 (n= 7, 0, 0, 0, 2)	36800 (± 26100)	999 (± 999)	10700 (± 1640)	999 (± 999)

End point values	LNP023 50 mg b.i.d. (4-week administration)			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 0, 2, 3, 10, 0)	16500 (± 5920)			
Day 113 (n= 7, 0, 0, 0, 2)	999 (± 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics in urine: renal plasma clearance derived from 24 hour urine sample

End point title	Pharmacokinetics in urine: renal plasma clearance derived from 24 hour urine sample[14]

End point description:

Pharmacokinetics of LNP023 in urine: Renal plasma clearance derived from 24 hour urine sample

End point type	Secondary

End point timeframe:

Day 113

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this outcome.

End point values	LNP023 200 mg b.i.d.			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: L/hr				
arithmetic mean (standard deviation)	1.19 (± 0.668)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 29 weeks post treatment, up to maximum duration of 53 weeks.

Adverse event reporting additional description:

Any sign or symptom that occurs during the conduct of the trial and the safety follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	LNP023 10/50 mg b.i.d.

Reporting group description:

As per protocol V00, participants took LNP023 10 mg orally b.i.d. for 4 weeks followed by LNP023 50 mg orally b.i.d. for 20 weeks

Reporting group title	LNP023 200 mg b.i.d. (combination of 25/200 mg, 50/200 mg)

Reporting group description:

Combination of the LNP023 25/200 mg b.i.d. and 50/200 mg b.i.d. groups. Under protocol V00, participants took LNP023 25 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks. Under protocol v01, participants took LNP023 50 mg orally b.i.d. for 4 weeks followed by LNP023 200 mg orally b.i.d. for 20 weeks.

Reporting group title	Pooled LNP023

Reporting group description:

Combination of the LNP023 10/50 mg b.i.d., 25/200 mg b.i.d. and 50/200 mg b.i.d. groups.

Reporting group title	Rituximab 1 g i.v.

Reporting group description:

Rituximab 1 g i.v. at Day 1 and Day 15

Reporting group title	Total

Reporting group description:

Total

Serious adverse events	LNP023 10/50 mg b.i.d.	LNP023 200 mg b.i.d. (combination of 25/200 mg, 50/200 mg)	Pooled LNP023
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	3 / 22 (13.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (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 pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Rituximab 1 g i.v.	Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 15 (20.00%)	6 / 37 (16.22%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 15 (6.67%)	2 / 37 (5.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	LNP023 10/50 mg b.i.d.	LNP023 200 mg b.i.d. (combination of 25/200 mg, 50/200 mg)	Pooled LNP023
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	13 / 19 (68.42%)	15 / 22 (68.18%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 22 (9.09%)
occurrences (all)	0	4	4
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Oedema peripheral			

subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Epididymal cyst			
subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Hypersomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Headache			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	3 / 22 (13.64%)
occurrences (all)	0	3	3
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dyspepsia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Inguinal hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 22 (9.09%)
occurrences (all)	0	3	3
Bone hypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1

Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)	1 / 19 (5.26%)	2 / 22 (9.09%)
occurrences (all)	1	1	2
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	3 / 22 (13.64%)
occurrences (all)	0	3	3
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Coronavirus infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gout			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Vitamin B12 deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 22 (4.55%)
occurrences (all)	0	1	1

Non-serious adverse events	Rituximab 1 g i.v.	Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 15 (46.67%)	22 / 37 (59.46%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	4	
Influenza like illness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Epididymal cyst			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	

Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	2	2	
Epistaxis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Infusion related reaction			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Head injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Fall			

subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Post-traumatic pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hypersomnia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	0 / 15 (0.00%)	3 / 37 (8.11%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Abdominal pain lower			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Inguinal hernia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Epigastric discomfort			

subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Rash maculo-papular			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	3	
Bone hypertrophy			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 15 (6.67%)	3 / 37 (8.11%)	
occurrences (all)	2	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	4 / 37 (10.81%)	
occurrences (all)	1	4	
Lower respiratory tract infection			

subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Coronavirus infection			
subjects affected / exposed	1 / 15 (6.67%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Respiratory tract infection viral			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Gout			
subjects affected / exposed	2 / 15 (13.33%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Hypokalaemia			
subjects affected / exposed	1 / 15 (6.67%)	3 / 37 (8.11%)	
occurrences (all)	1	3	
Vitamin B12 deficiency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2021	The main purpose of the global amendment was to align with study results obtained from ongoing trials with LNP023 in other indications which support best efficacy results with LNP023 at dose levels of 200mg b.i.d. LNP023 low dose arm (10/50mg) was removed from this study and the first portion of the high dose arm was modified from 25 to 50mg b.i.d for 4 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: