



## Clinical trial results:

**An open-label, non-randomized study on efficacy, pharmacokinetics, pharmacodynamics, safety and tolerability of LNP023 in two patient populations with C3 glomerulopathy**

### Summary

EudraCT number	2017-000889-29
Trial protocol	GB ES DE FR IT
Global end of trial date	23 April 2021

### Results information

Result version number	v2 (current)
This version publication date	16 May 2024
First version publication date	08 May 2022
Version creation reason	

### Trial information

#### Trial identification

Sponsor protocol code	CLNP023X2202
-----------------------	--------------

#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03832114
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Eswatini,
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	23 April 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	23 April 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this trial was to evaluate the efficacy of LNP023 in reducing proteinuria at Week 12 (Cohort A) and to assess histopathological changes in kidney biopsies at Week 12 (Cohort B).

Protection of trial subjects:

This 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	20 February 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	France: 6
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	27
EEA total number of subjects	15

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)	25
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 27 patients (16 patients in Cohort A and 11 patients in Cohort B) were enrolled and treated in the treatment period 1. All 27 patients completed the study and there were no patients who discontinued the study.

### Pre-assignment

Screening details:

A total of 27 patients (16 patients in Cohort A and 11 patients in Cohort B) were enrolled and treated in the treatment period 1. All 27 patients completed the study and there were no patients who discontinued the study.

### Period 1

Period 1 title	Dose Escalation/200mg b.i.d treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d

Arm description:

Cohort A - no kidney transplant C3G patients who have not received a kidney transplant and have reduced C3 blood levels

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:

A starting dose of LNP023 of 10 mg twice daily (b.i.d.) was administered during the first treatment week (Week 1), followed by 25 mg b.i.d. (Week 2), 100 mg b.i.d. for 1 week (Week 3) and ending at 200 mg b.i.d. on Week 4. The 200 mg b.i.d. dose was continued for additional 8 weeks for a total duration of 9 weeks

<b>Arm title</b>	Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d
------------------	--

Arm description:

Cohort B - kidney transplant C3G patients who have received a kidney transplant and have C3G recurrence

Arm type	Experimental
Investigational medicinal product name	iptacopan
Investigational medicinal product code	CLNP023
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A starting dose of LNP023 of 10 mg twice daily (b.i.d.) was administered during the first treatment week (Week 1), followed by 25 mg b.i.d. (Week 2), 100 mg b.i.d. for 1 week (Week 3) and ending at 200 mg b.i.d. on Week 4. The 200 mg b.i.d. dose was continued for additional 8 weeks for a total duration of 9 weeks

<b>Number of subjects in period 1</b>	Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d	Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d
Started	16	11
Completed	16	11

## Baseline characteristics

### Reporting groups

Reporting group title	Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d
Reporting group description: Cohort A - no kidney transplant C3G patients who have not received a kidney transplant and have reduced C3 blood levels	
Reporting group title	Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d
Reporting group description: Cohort B - kidney transplant C3G patients who have received a kidney transplant and have C3G recurrence	

Reporting group values	Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d	Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d	Total
Number of subjects	16	11	27
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)	16	9	25
From 65-84 years	0	2	2
85 years and over	0	0	0
Age Continuous			
Age in Years			
Units: Years			
median	22.0	31.0	
full range (min-max)	18 to 59	18 to 70	-
Sex: Female, Male			
Units: Participants			
Female	6	3	9
Male	10	8	18
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska	0	1	1
Black or African American	0	1	1
White	16	9	25

### Subject analysis sets

Subject analysis set title	Cohort A - no kidney transplant
Subject analysis set type	Full analysis
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	

Subject analysis set title	Cohort B - kidney transplant
Subject analysis set type	Full analysis
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence.	
Subject analysis set title	Cohort A - no kidney transplant - LNP023 10mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d. of LNP023 during the first treatment week (Week 1) of the dose escalation phase	
Subject analysis set title	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d. of LNP023 during the second treatment week (Week 2) of the dose escalation phase	
Subject analysis set title	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	
Subject analysis set title	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).	
Subject analysis set title	Cohort B - kidney transplant - LNP023 10mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d. of LNP023 during the first treatment week (Week 1) of the dose escalation phase	
Subject analysis set title	Cohort B - kidney transplant - LNP023 25 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d. of LNP023 during the second treatment week (Week 2) of the dose escalation phase	
Subject analysis set title	Cohort B - kidney transplant - LNP023 100 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	
Subject analysis set title	Cohort B - kidney transplant - LNP023 200 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).	

Reporting group values	Cohort A - no kidney transplant	Cohort B - kidney transplant	Cohort A - no kidney transplant - LNP023 10mg b.i.d.
Number of subjects	16	11	15

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous			
Age in Years			
Units: Years			
median	22.0	31.0	
full range (min-max)	18 to 59	18 to 70	
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Black or African American White			

<b>Reporting group values</b>	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Number of subjects	16	16	15
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous			
Age in Years			
Units: Years			
median			
full range (min-max)			
Sex: Female, Male			
Units: Participants			
Female			
Male			



Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Black or African American White			

Reporting group values	Cohort B - kidney transplant - LNP023 10mg b.i.d.	Cohort B - kidney transplant - LNP023 25 mg b.i.d.	Cohort B - kidney transplant - LNP023 100 mg b.i.d.
Number of subjects	11	11	11
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous			
Age in Years			
Units: Years median full range (min-max)			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Black or African American White			

Reporting group values	Cohort B - kidney transplant - LNP023 200 mg b.i.d.		
Number of subjects	9		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			

85 years and over			
-------------------	--	--	--

Age Continuous			
Age in Years			
Units: Years			
median			
full range (min-max)			
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska			
Black or African American			
White			

## End points

### End points reporting groups

Reporting group title	Cohort A: Dose Escalation/LNP023 Treatment 200 mg b.i.d
Reporting group description: Cohort A - no kidney transplant C3G patients who have not received a kidney transplant and have reduced C3 blood levels	
Reporting group title	Cohort B - Dose Escalation/LNP023 Treatment 200 mg b.i.d
Reporting group description: Cohort B - kidney transplant C3G patients who have received a kidney transplant and have C3G recurrence	
Subject analysis set title	Cohort A - no kidney transplant
Subject analysis set type	Full analysis
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels.	
Subject analysis set title	Cohort B - kidney transplant
Subject analysis set type	Full analysis
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence.	
Subject analysis set title	Cohort A - no kidney transplant - LNP023 10mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	
Subject analysis set title	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	
Subject analysis set title	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	
Subject analysis set title	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have not received a kidney transplant and have reduced C3 blood levels. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase, and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).	
Subject analysis set title	Cohort B - kidney transplant - LNP023 10mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 10 mg b.i.d.of LNP023 during the first treatment week (Week 1) of the dose escalation phase	
Subject analysis set title	Cohort B - kidney transplant - LNP023 25 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 25 mg b.i.d.of LNP023 during the second treatment week (Week 2) of the dose escalation phase	
Subject analysis set title	Cohort B - kidney transplant - LNP023 100 mg b.i.d.

Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 100 mg b.i.d. of LNP023 during the third treatment week (Week 3) of the dose escalation phase	
Subject analysis set title	Cohort B - kidney transplant - LNP023 200 mg b.i.d.
Subject analysis set type	Per protocol
Subject analysis set description: C3G patients who have received a kidney transplant and have C3G recurrence. Patients received 200 mg b.i.d. of LNP023 during the fourth treatment week (Week 4) of the dose escalation phase and continued receiving 200 mg b.i.d. for additional 8 weeks (Patients received 200 mg b.i.d. of LNP023 a total of 9 weeks).	

### Primary: Cohort B: Change from baseline in C3 Deposit

End point title	Cohort B: Change from baseline in C3 Deposit <sup>[1]</sup>
End point description: Histopathological changes in kidney biopsies as assessed by change from baseline in C3 Deposit Score (based on immunofluorescence microscopy)	
End point type	Primary
End point timeframe: Week 12	
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: No statistical analyses for this end point	

End point values	Cohort B - kidney transplant			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Percentage change				
median (confidence interval 80%)	-2.50 (-3.75 to -0.75)			

### Statistical analyses

No statistical analyses for this end point

### Primary: Cohort A: Change from baseline in Urine Protein to Creatinine concentration Ratio (UPCR)

End point title	Cohort A: Change from baseline in Urine Protein to Creatinine concentration Ratio (UPCR) <sup>[2]</sup>
End point description: Change in proteinuria assessed by ratio to baseline of UPCR derived from 24h urine collection	
End point type	Primary
End point timeframe: Week 12	
Notes: [2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analyses for this end point	

End point values	Cohort A - no kidney transplant			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: ratio				
geometric mean (confidence interval 80%)	0.55 (0.46 to 0.65)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in Urine Protein (UP) Excretion

End point title	Change from baseline in Urine Protein (UP) Excretion
End point description:	
Ratio to baseline UP excretion derived from 24 hour urine collection	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: ratio				
geometric mean (confidence interval 80%)	0.57 (0.47 to 0.68)	1.00 (0.75 to 1.33)		

## Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description:	
Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0011
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.57

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.68

<b>Statistical analysis title</b>	Overall Study
Statistical analysis description:	
Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0016
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.66
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.56
upper limit	0.77

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description:	
Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[3]</sup>
P-value	= 0.9998
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.75
upper limit	1.33

Notes:

[3] - Statistical Analysis presented for Cohort B below only. Cohort A is presented in a separate table.

## Secondary: Change from baseline in Urine Protein Creatinine Concentration Ratio (UPCR)

End point title	Change from baseline in Urine Protein Creatinine Concentration Ratio (UPCR)
-----------------	---

End point description:	
Ratio to baseline UPCR derived from 24 hour urine collection	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: ratio				
geometric mean (confidence interval 80%)	0.55 (0.46 to 0.65)	0.79 (0.49 to 1.28)		

## Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description:	
Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other <sup>[4]</sup>
P-value	= 0.0003
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.55
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.46
upper limit	0.65

Notes:

[4] - Statistical Analysis is presented below for Cohort A only. Cohort B is presented in a separate table.

Statistical analysis title	Overall Analysis
Statistical analysis description:	
Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	Mixed Model of Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.59

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.51
upper limit	0.69

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other <sup>[5]</sup>
P-value	= 0.4766
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.79
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.49
upper limit	1.28

Notes:

[5] - Statistical Analysis is presented for Cohort B below. Cohort A is in a separate table.

### Secondary: Change from baseline in Urine Albumin Creatinine concentration Ratio (UACR) Excretion

End point title	Change from baseline in Urine Albumin Creatinine concentration Ratio (UACR) Excretion
End point description: Ratio to baseline UACR excretion derived from 24 hour urine collection	
End point type	Secondary
End point timeframe: Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: ratio				
geometric mean (confidence interval 80%)	0.55 (0.47 to 0.64)	0.61 (0.30 to 1.27)		



## Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other <sup>[6]</sup>
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.55
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.64

Notes:

[6] - Statistical Analysis presented for Cohort A below only. Cohort B is presented in a separate table.

Statistical analysis title	Overall Study
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.51
upper limit	0.71

Statistical analysis title	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other <sup>[7]</sup>
P-value	= 0.3707
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.61

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.3
upper limit	1.27

Notes:

[7] - Statistical Analysis presented for Cohort B only below. Cohort A is presented in a separate table.

### Secondary: Change from baseline in estimated glomerular filtration rate (eGFR)

End point title	Change from baseline in estimated glomerular filtration rate (eGFR)
End point description: Effect of LNP023 on estimated glomerular filtration rate (eGFR)	
End point type	Secondary
End point timeframe: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: ml/min				
arithmetic mean (confidence interval 80%)	2.59 (0.12 to 5.06)	-0.61 (-3.36 to 2.15)		

### Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[8]</sup>
P-value	= 0.1795
Method	Mixed Model of Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	2.59
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.12
upper limit	5.06

Notes:

[8] - tatistical analysis is presented for Cohort A below only. Cohort B is presented in a separate table.

<b>Statistical analysis title</b>	Overall
Statistical analysis description:	
Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3754
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.32
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.59
upper limit	3.22

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description:	
Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[9]</sup>
P-value	= 0.7763
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-0.61
Confidence interval	
level	Other: 0.78 %
sides	2-sided
lower limit	-3.36
upper limit	2.15

Notes:

[9] - Statistical Analysis presented for Cohort B below only. Cohort A is presented in a separate table .

<b>Secondary: Change from baseline change in Urinary Albumin (UA) Excretion</b>	
End point title	Change from baseline change in Urinary Albumin (UA) Excretion
End point description:	
Ratio to baseline UA excretion derived from 24 hour urine collection	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: ratio				
geometric mean (confidence interval 80%)	0.57 (0.47 to 0.70)	0.81 (0.67 to 0.98)		

## Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[10]</sup>
P-value	= 0.0018
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.57
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.7

Notes:

[10] - Statistical Analysis is presented for Cohort A below only. Cohort A is presented in a separate table.

Statistical analysis title	Overall Study
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Mixed Model Repeated Measure (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.67
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.57
upper limit	0.79

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[11]</sup>
P-value	= 0.1632
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.81
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.67
upper limit	0.98

Notes:

[11] - Statistical Analysis is presented below for Cohort B only. Cohort A is presented in a separate table.

### Secondary: Change from baseline in serum creatinine

End point title	Change from baseline in serum creatinine
End point description: The effect of LNP023 on renal function - serum creatinine	
End point type	Secondary
End point timeframe: Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: mmol/L				
arithmetic mean (confidence interval 80%)	-5.04 (-9.36 to -0.72)	7.17 (-1.79 to 16.13)		

### Statistical analyses

<b>Statistical analysis title</b>	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[12]</sup>
P-value	= 0.1364
Method	Mixed Model Repeated Measuers (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-5.04
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-9.36
upper limit	-0.72

Notes:

[12] - Statistical Analysis is presented for Cohort A below only. Cohort B is presented in a separate table.

<b>Statistical analysis title</b>	Overall
Statistical analysis description:	
Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8352
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-0.77
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-5.56
upper limit	4.01

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description:	
Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other <sup>[13]</sup>
P-value	= 0.3038
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	7.17
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.79
upper limit	16.13

Notes:

[13] - This analysis represents only Cohort B, as Cohort A is in a separate table.

### Secondary: Change from baseline in Urine Protein to Creatinine Concentration Ratio (UPCR) First Morning Void

End point title	Change from baseline in Urine Protein to Creatinine Concentration Ratio (UPCR) First Morning Void
End point description:	Ratio to baseline of UPCR reduction derived from total cumulative urinary excretion first morning void
End point type	Secondary
End point timeframe:	Week 9: Day 64

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	7		
Units: ratio				
geometric mean (confidence interval 80%)	0.56 (0.48 to 0.65)	0.99 (0.76 to 1.28)		

### Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description:	Day 64
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other <sup>[14]</sup>
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.56
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.48
upper limit	0.65

Notes:

[14] - Statistical Analysis is presented for Cohort A below. Cohort B is in a separate table

Statistical analysis title	Overall Analysis
Statistical analysis description:	Overall- Day 64
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.64
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.56
upper limit	0.72

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description:	
Day 64	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other <sup>[15]</sup>
P-value	= 0.9544
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.99
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.76
upper limit	1.28

Notes:

[15] - Statistical Analysis is presented for Cohort B below. Cohort A is presented in a separate table

### Secondary: Change from baseline in creatinine clearance

End point title	Change from baseline in creatinine clearance
End point description:	
The effect of LNP023 on renal function - creatinine clearance	
End point type	Secondary
End point timeframe:	
Week 12: Day 84	



End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	8		
Units: mL/min				
geometric mean (confidence interval 80%)	1.07 (0.99 to 1.17)	1.20 (0.83 to 1.72)		

## Statistical analyses

Statistical analysis title	Cohort A
Statistical analysis description: Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other <sup>[16]</sup>
P-value	= 0.2752
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.07
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.99
upper limit	1.17

Notes:

[16] - The analysis only represents Cohort A, as Cohort B is presented in a separate table .

Statistical analysis title	Overall
Statistical analysis description: Overall- Day 84	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1963
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1
upper limit	1.2

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description: Day 84	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other <sup>[17]</sup>
P-value	= 0.476
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.83
upper limit	1.72

Notes:

[17] - Statistical analysis presented for Cohort B only. Cohort A is presented in a separate table.

### Secondary: Change from baseline in Urine Albumin to Creatinine Concentration Ratio (UACR) First Morning Void

End point title	Change from baseline in Urine Albumin to Creatinine Concentration Ratio (UACR) First Morning Void
End point description: UACR reduction derived from total cumulative urinary excretion first morning void	
End point type	Secondary
End point timeframe: Week 9: Day 64	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	7		
Units: g/mol				
geometric mean (confidence interval 80%)	0.59 (0.50 to 0.69)	0.87 (0.60 to 1.26)		

### Statistical analyses

<b>Statistical analysis title</b>	Cohort A
Statistical analysis description: Day 64	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other <sup>[18]</sup>
P-value	< 0.0001
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.59
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.5
upper limit	0.69

Notes:

[18] - tatistical Analysis is presented below for Cohort A only. Cohort B is presented in a separate table

<b>Statistical analysis title</b>	Overall Analysis
Statistical analysis description:	
Overall- Day 64	
Comparison groups	Cohort A - no kidney transplant v Cohort B - kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	0.63
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.54
upper limit	0.73

<b>Statistical analysis title</b>	Cohort B
Statistical analysis description:	
Day 64	
Comparison groups	Cohort B - kidney transplant v Cohort A - no kidney transplant
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other <sup>[19]</sup>
P-value	= 0.6209
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Median difference (final values)
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.6
upper limit	1.26

Notes:

[19] - Statistical Analysis is presented for Cohort B only below. Cohort A is presented in a separate table.

### Secondary: Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUClast (AUC)

End point title	Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUClast (AUC)
-----------------	---

End point description:

The area under the plasma concentration-time curve calculated from time zero to the last quantifiable concentration point (hr\*ng/mL)

End point type	Secondary
----------------	-----------

End point timeframe:

Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)

End point values	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	16	16	15
Units: hr*ng/mL				
arithmetic mean (standard deviation)	3690 (± 693)	5790 (± 1630)	13200 (± 4410)	20300 (± 8180)

End point values	Cohort B - kidney transplant - LNP023 10mg b.i.d.	Cohort B - kidney transplant - LNP023 25 mg b.i.d.	Cohort B - kidney transplant - LNP023 100 mg b.i.d.	Cohort B - kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	11	9
Units: hr*ng/mL				
arithmetic mean (standard deviation)	4560 (± 2060)	7880 (± 3830)	19600 (± 12100)	28100 (± 15900)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUCtau (AUC)

End point title	Pharmacokinetics of LNP023 Area under the Plasma-concentration-time curve AUCtau (AUC)
-----------------	--

End point description:

The area under the plasma concentration-time curve calculated to the end of the dosing interval (hr\*ng/mL)

End point type	Secondary
End point timeframe:	
Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)	

End point values	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	16	16	15
Units: hr*ng/mL				
arithmetic mean (standard deviation)	5020 (± 1110)	7970 (± 2250)	17800 (± 5800)	26900 (± 10900)

End point values	Cohort B - kidney transplant - LNP023 10mg b.i.d.	Cohort B - kidney transplant - LNP023 25 mg b.i.d.	Cohort B - kidney transplant - LNP023 100 mg b.i.d.	Cohort B - kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	11	9
Units: hr*ng/mL				
arithmetic mean (standard deviation)	6300 (± 3000)	10700 (± 5310)	26600 (± 16500)	37700 (± 22000)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Observed maximum concentration after drug administration (Cmax)

End point title	Observed maximum concentration after drug administration (Cmax)
End point description:	
The observed maximum plasma concentration (ng/mL)	
End point type	Secondary
End point timeframe:	
Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)	

End point values	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	16	16	15
Units: ng/mL				
arithmetic mean (standard deviation)	637 (± 97.1)	941 (± 278)	2270 (± 805)	3600 (± 1230)

End point values	Cohort B - kidney transplant - LNP023 10mg b.i.d.	Cohort B - kidney transplant - LNP023 25 mg b.i.d.	Cohort B - kidney transplant - LNP023 100 mg b.i.d.	Cohort B - kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	11	9
Units: ng/mL				
arithmetic mean (standard deviation)	713 (± 292)	1280 (± 552)	3250 (± 1790)	4700 (± 2200)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to reach the maximum plasma concentration (Tmax)

End point title	Time to reach the maximum plasma concentration (Tmax)
-----------------	---

End point description:

The time to reach peak or maximum concentration (hr)

End point type	Secondary
----------------	-----------

End point timeframe:

Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)

End point values	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A -no kidney transplant - LNP023 100 mg b.i.d.	Cohort A -no kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	16	16	15
Units: hr				
median (full range (min-max))	2.00 (0.800 to 6.00)	2.00 (0.900 to 4.00)	2.00 (0.500 to 4.00)	2.00 (1.00 to 4.00)

End point values	Cohort B -	Cohort B -	Cohort B -	Cohort B -
------------------	------------	------------	------------	------------

	kidney transplant - LNP023 10mg b.i.d.	kidney transplant - LNP023 25 mg b.i.d.	kidney transplant - LNP023 100 mg b.i.d.	kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	11	9
Units: hr				
median (full range (min-max))	2.00 (1.00 to 4.00)	2.00 (1.00 to 6.00)	2.00 (1.00 to 4.00)	2.00 (1.00 to 4.00)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary of Change from Baseline Complement C3 biomarker in serum

End point title	Summary of Change from Baseline Complement C3 biomarker in serum
End point description: To assess the effect of LNP023 on alternative complement pathway hyperactivity.	
End point type	Secondary
End point timeframe: Baseline, Day 1, Day 7, Day 14, Day 21, Day 28, Day 36, Day 64, Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	10		
Units: g/L				
arithmetic mean (standard deviation)				
Day 1 pre-dose	0.0 (± 0.06)	0.0 (± 0.12)		
Day 7 - pre-dose	0.1 (± 0.10)	0.2 (± 0.22)		
Day 14 - pre-dose	0.3 (± 0.17)	0.4 (± 0.29)		
Day 21 - pre-dose	0.5 (± 0.25)	0.4 (± 0.33)		
Day 28 - pre-dose	0.5 (± 0.29)	0.4 (± 0.27)		
Day 36 - pre-dose	0.6 (± 0.28)	0.4 (± 0.32)		
Day 64 - pre-dose	0.6 (± 0.27)	0.4 (± 0.26)		
Day 84 - pre-dose	0.6 (± 0.30)	0.5 (± 0.26)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with hematuria

End point title	Number of patients with hematuria
-----------------	-----------------------------------

End point description: The effect of LNP023 on renal function - hematuria	
End point type	Secondary
End point timeframe: Week 12: Day 84	

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: participants				
Week 12: Day 84: <9 rbc/hpf n (%)	10	3		
Week 12: Day 84: >= 9 to <=50 rbc/hpf n (%)	0	0		
Week 12: Day 84: >50 rbc/hpf n (%)	0	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Observed minimum concentration after drug administration (Ctrough)

End point title	Observed minimum concentration after drug administration (Ctrough)
End point description: The concentration that is just prior to the beginning of, or at the end, of a dosing interval (ng/mL)	
End point type	Secondary
End point timeframe: Day 7, Day 14, Day 21, Day 28 (pre-dose, 0.5h, 1h, 2h, 4h, 6h, 8h post dose) and Day 36, Day 64 and Day 84 (pre-dose)	

End point values	Cohort A - no kidney transplant - LNP023 10mg b.i.d.	Cohort A - no kidney transplant - LNP023 25 mg b.i.d.	Cohort A - no kidney transplant - LNP023 100 mg b.i.d.	Cohort A - no kidney transplant - LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	16	16	15
Units: ng/mL				
arithmetic mean (standard deviation)	314 (± 133)	519 (± 133)	1090 (± 408)	1480 (± 653)

End point values	Cohort B - kidney transplant -	Cohort B - kidney transplant -	Cohort B - kidney transplant -	Cohort B - kidney transplant -
------------------	--------------------------------	--------------------------------	--------------------------------	--------------------------------



	LNP023 10mg b.i.d.	LNP023 25 mg b.i.d.	LNP023 100 mg b.i.d.	LNP023 200 mg b.i.d.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	11	9
Units: ng/mL				
arithmetic mean (standard deviation)	417 (± 237)	644 (± 325)	1650 (± 1010)	2180 (± 1610)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Ratio to baseline summary of Plasma Bb

End point title	Ratio to baseline summary of Plasma Bb
End point description:	To assess the relationship between LNP023 dose and pharmacodynamic biomarker levels of blood Bb
End point type	Secondary
End point timeframe:	Baseline, Day 1, Day 7, Day 14, Day 21, Day 28, Day 36, Day 64, Day 84

End point values	Cohort A - no kidney transplant	Cohort B - kidney transplant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	10		
Units: Ratio of plasma Bb				
arithmetic mean (standard deviation)				
Day 1 pre-dose	101.8 (± 45.18)	109.7 (± 34.08)		
Day 7 pre-dose	102.4 (± 40.47)	83.6 (± 27.73)		
Day 14 pre-dose	104.4 (± 43.35)	81.8 (± 39.34)		
Day 21 pre-dose	97.0 (± 58.06)	66.4 (± 22.95)		
Day 28 pre-dose	90.2 (± 46.24)	71.5 (± 29.52)		
Day 36 pre-dose	102.5 (± 54.06)	65.9 (± 31.20)		
Day 64 pre-dose	116.8 (± 59.76)	73.2 (± 29.62)		
Day 84 pre-dose	116.6 (± 57.85)	76.3 (± 35.84)		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events

Adverse event reporting additional description:

Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.0
--------------------	------

### Reporting groups

Reporting group title	Cohort A - Run-in Phase
-----------------------	-------------------------

Reporting group description:

Cohort A - Run-in Phase

Reporting group title	Cohort A - Dose Escalation Phase
-----------------------	----------------------------------

Reporting group description:

Cohort A - Dose Escalation Phase

Reporting group title	Cohort B - LNP023 200mg b.i.d.
-----------------------	--------------------------------

Reporting group description:

Cohort B - LNP023 200mg b.i.d.

Reporting group title	Cohort B - Run-in Phase
-----------------------	-------------------------

Reporting group description:

Cohort B - Run-in Phase

Reporting group title	Cohort B - Dose Escalation Phase
-----------------------	----------------------------------

Reporting group description:

Cohort B - Dose Escalation Phase

Reporting group title	Cohort A - LNP023 200mg b.i.d.
-----------------------	--------------------------------

Reporting group description:

Cohort A - LNP023 200mg b.i.d.

Serious adverse events	Cohort A - Run-in Phase	Cohort A - Dose Escalation Phase	Cohort B - LNP023 200mg b.i.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	2 / 11 (18.18%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Cohort B - Run-in Phase	Cohort B - Dose Escalation Phase	Cohort A - LNP023 200mg b.i.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (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
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (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

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

<b>Non-serious adverse events</b>	Cohort A - Run-in Phase	Cohort A - Dose Escalation Phase	Cohort B - LNP023 200mg b.i.d.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	6 / 16 (37.50%)	6 / 11 (54.55%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Spider vein			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Psychiatric disorders Intentional self-injury subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Adjustment disorder with depressed mood subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	1 / 11 (9.09%) 1
Blood luteinising hormone increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Lipase increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Body temperature increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Cardiac disorders			

Palpitations subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Nervous system disorders			
Anosmia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Dysgeusia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Headache subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Normochromic normocytic anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Eye disorders			
Conjunctival hyperaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1

Vomiting subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	1 / 11 (9.09%) 1
Dyspepsia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Skin and subcutaneous tissue disorders Skin discolouration subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Respiratory tract infection viral subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Influenza			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Hordeolum subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1
Metabolism and nutrition disorders			
Gout subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Dyslipidaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	2 / 11 (18.18%) 2
Iron deficiency subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0

<b>Non-serious adverse events</b>	Cohort B - Run-in Phase	Cohort B - Dose Escalation Phase	Cohort A - LNP023 200mg b.i.d.
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 11 (0.00%)	5 / 11 (45.45%)	8 / 16 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 11 (9.09%) 1	0 / 16 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 11 (9.09%) 1	1 / 16 (6.25%) 1
Spider vein subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Psychiatric disorders			
Intentional self-injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood luteinising hormone increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nervous system disorders			



Anosmia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 11 (9.09%) 1	0 / 16 (0.00%) 0
Skin and subcutaneous tissue disorders Skin discolouration subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	1 / 16 (6.25%) 1
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	1 / 16 (6.25%) 1
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	1 / 16 (6.25%) 1
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0
Respiratory tract infection viral subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 11 (9.09%) 1	0 / 16 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0
Hordeolum			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 11 (0.00%) 0	0 / 16 (0.00%) 0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dyslipidaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2018	Non-Substantial Amendment: text added to indicate patients must receive vaccinations against N. meningitidis, S. pneumoniae and H. influenzae prior to first dosing.
22 February 2019	Germany: The purpose of this local protocol amendment was to modify the study stopping rules for drug related events and to clarify if the study was halted the restart would be documented by a substantial amendment as per Health Authority questions.
20 August 2019	The purpose of this amendment was to include a second treatment period (Treatment period 2) to enable the prolongation of treatment by 12 weeks for any patient.
07 February 2020	The purpose of this amendment was mainly to correct the estimation of the blood sample volume to be collected, confirming that there is no increased risk for the patient.

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported