Clinical trial results:
An open label, single arm, multiple dose study to assess efficacy, safety, pharmacokinetics and pharmacodynamics of LNP023 when administered in addition to Standard of Care (SoC) in patients with paroxysmal nocturnal hemoglobinuria (PNH) with signs of active hemolysis

Summary

EudraCT number	2017-000888-33
Trial protocol	DE FR IT
Global end of trial date	28 February 2022

Results information

Result version number	v1 (current)
This version publication date	08 March 2023
First version publication date	08 March 2023

Trial information

Trial identification

Sponsor protocol code	CLNP023X2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03439839
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	28 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of iptacopan on the reduction of chronic hemolysis in PNH patients when administered in addition to SoC (monoclonal antibody with anti C5 activity).
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.

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	09 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 8
Worldwide total number of subjects	16
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)	15
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 3 investigative sites in 3 countries: France (1), Italy (1) and Germany (1).

Pre-assignment

Screening details:

All patients needed to complete vaccinations against N. meningitidis, S. pneumoniae and H. influenzae at least 4 weeks prior to starting LNP023 treatment. If LNP023 treatment had to start earlier than 4 weeks post vaccination, prophylactic antibiotic treatment was initiated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: LNP023 200mg bid + SoC

Arm description:

Orally administered iptacopan 200 mg b.i.d. in Part 1 and Part 2 in addition to SoC.

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

Dosage and administration details:

Oral iptacopan hard gelatin capsule 200 mg b.i.d

Arm title	Cohort 2: LNP023 50mg/200mg bid + SoC

Arm description:

Orally administered iptacopan 50 mg b.i.d. for a minimum of 2 weeks in addition to SoC; this could be increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values.

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

Dosage and administration details:

Orally administered iptacopan 50 mg b.i.d. for a minimum of 2 weeks in addition to SoC; this could be increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values.

Number of subjects in period 1	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC
Started	10	6
Completed	7	6
Not completed	3	0
Adverse event, serious fatal	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: LNP023 200mg bid + SoC
Reporting group description:	
Orally administered iptacopan 200 mg b.i.d. in Part 1 and Part 2 in addition to SoC.	
Reporting group title	Cohort 2: LNP023 50mg/200mg bid + SoC
Reporting group description:	
Orally administered iptacopan 50 mg b.i.d. for a minimum of 2 weeks in addition to SoC; this could be increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values.	

Reporting group values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC	Total
Number of subjects	10	6	16
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	9	6	15
>=65 years	1	0	1
Age Continuous Units: years			
arithmetic mean	44.4	51.7	
standard deviation	± 15.57	± 9.83	-
Sex: Female, Male Units: participants			
Female	3	3	6
Male	7	3	10
Race/Ethnicity, Customized Units: Subjects			
Unknown	0	1	1
White	10	5	15

End points

End points reporting groups

Reporting group title	Cohort 1: LNP023 200mg bid + SoC
Reporting group description:	
Orally administered iptacopan 200 mg b.i.d. in Part 1 and Part 2 in addition to SoC.	
Reporting group title	Cohort 2: LNP023 50mg/200mg bid + SoC
Reporting group description:	
Orally administered iptacopan 50 mg b.i.d. for a minimum of 2 weeks in addition to SoC; this could be increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values.	
Subject analysis set title	Cohort 2: LNP023 25mg bid + SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orally administered iptacopan 25 mg b.i.d. at the respective visit due to dosing error	
Subject analysis set title	Cohort 2: LNP023 50mg bid + SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orally administered iptacopan 50 mg b.i.d. at the respective visit	
Subject analysis set title	Cohort 2: LNP023 200mg bid + SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orally administered iptacopan 200 mg b.i.d. at the respective visit	

Primary: Percent change from baseline in lactate dehydrogenase (LDH) level at Day 92

End point title	Percent change from baseline in lactate dehydrogenase (LDH) level at Day 92[1]
End point description:	
Serum LDH was used as an intravascular hemolysis marker to assess the effect of iptacopan on the reduction of chronic hemolysis in paroxysmal nocturnal hemoglobinuria (PNH) patients when administered in addition to SoC (monoclonal antibody with anti C5 activity) Baseline is defined as the mean of the last 3 measurements prior to dose administration. No statistical analysis was planned for this primary outcome.	
End point type	Primary
End point timeframe:	
Baseline and Day 92	

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 analysis was planned for this outcome.

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	5		
Units: Percentage of LDH				
arithmetic mean (confidence interval 90%)	-53.59 (-61.38 to -45.79)	-25.56 (-46.92 to -4.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in Lactate dehydrogenase (LDH) level

End point title	Absolute change from baseline in Lactate dehydrogenase (LDH) level

End point description:

Serum LDH was used as an intravascular hemolysis marker to assess the effect of iptacopan on the reduction of chronic hemolysis in paroxysmal nocturnal hemoglobinuria (PNH) patients when administered in addition to SoC (monoclonal antibody with anti C5 activity)

Baseline is defined as the mean of the last 3 measurements prior to dose administration.

End point type	Secondary

End point timeframe:

Baseline, day 8, 15, 29, 57 and 92

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: U/L				
arithmetic mean (confidence interval 90%)				
Day 8 (n= 10, 6)	-272.57 (-349.07 to -196.07)	-145.22 (-196.30 to -94.15)		
Day 15 (n= 10, 5)	-353.97 (-486.36 to -221.57)	-175.07 (-247.55 to -102.59)		
Day 29 (n= 10, 6)	-368.17 (-510.15 to -226.18)	-191.22 (-258.88 to -123.56)		
Day 57 (n= 10, 6)	-317.07 (-459.11 to -175.03)	-135.89 (-212.28 to -59.50)		
Day 92 (n= 9, 5)	-330.52 (-488.02 to -173.01)	-109.07 (-196.69 to -21.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in hemoglobin

End point title	Absolute change from baseline in hemoglobin

End point description:

Hemoglobin was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan.
Baseline is defined as the mean of all pre-dose measurements.

End point type	Secondary

End point timeframe:

Baseline; day 1, 2, 8, 15, 22, 29, 36, 43, 57, 71, 85, 92, 113, 127, 141, 155, 169, 197, 225, 253, 281, 309, 337, 393, 449, 505, 561, 617, 673, 729, 785, 841, 897, 953, 1009, 1065, 1121, 1177, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: g/L				
arithmetic mean (standard deviation)				
Day 1 (n= 10, 6)	-4.05 (± 8.750)	-6.67 (± 7.218)		
Day 2 (n= 10, 6)	-3.65 (± 7.638)	-8.06 (± 6.830)		
Day 8 (n= 10, 6)	12.85 (± 9.228)	20.11 (± 13.475)		
Day 15 (n= 10, 6)	20.25 (± 10.122)	26.44 (± 10.047)		
Day 22 (n= 10, 6)	24.15 (± 11.898)	35.11 (± 11.065)		
Day 29 (n= 10, 6)	28.25 (± 13.131)	35.11 (± 10.141)		
Day 36 (n= 10, 6)	29.55 (± 12.166)	33.94 (± 10.062)		
Day 43 (n= 10, 6)	26.15 (± 12.571)	31.11 (± 7.428)		
Day 57 (n= 10, 6)	27.05 (± 10.855)	35.94 (± 10.804)		
Day 71 (n= 8, 4)	24.53 (± 12.259)	28.54 (± 8.080)		
Day 85 (n= 10, 3)	28.65 (± 15.722)	30.72 (± 15.008)		
Day 92 (n= 10, 5)	31.85 (± 14.543)	32.43 (± 14.584)		
Day 113 (n= 9, 5)	30.14 (± 14.831)	32.43 (± 11.092)		
Day 127 (n= 9, 4)	33.92 (± 16.882)	38.92 (± 13.519)		
Day 141 (n= 10, 5)	28.05 (± 17.088)	37.23 (± 15.802)		
Day 155 (n= 8, 5)	28.28 (± 17.370)	37.83 (± 12.287)		
Day 169 (n= 10, 5)	27.05 (± 17.253)	39.43 (± 11.174)		
Day 197 (n= 10, 3)	28.95 (± 15.429)	31.89 (± 16.385)		
Day 225 (n= 10, 3)	28.65 (± 17.258)	28.67 (± 7.147)		

Day 253 (n= 10, 4)	26.95 (± 18.015)	28.17 (± 12.039)		
Day 281 (n= 9, 4)	29.91 (± 18.351)	45.54 (± 16.168)		
Day 309 (n= 9, 4)	27.17 (± 15.152)	36.29 (± 9.866)		
Day 337 (n= 9, 4)	26.28 (± 16.733)	32.50 (± 10.700)		
Day 393 (n= 9, 4)	28.47 (± 18.801)	39.79 (± 12.930)		
Day 449 (n= 8, 5)	31.22 (± 18.573)	37.93 (± 10.547)		
Day 505 (n= 7, 6)	24.89 (± 13.435)	44.28 (± 18.271)		
Day 561 (n= 6, 5)	29.25 (± 18.665)	40.13 (± 11.653)		
Day 617 (n= 7, 6)	32.23 (± 18.335)	42.78 (± 17.771)		
Day 673 (n= 5, 5)	38.42 (± 13.407)	38.13 (± 15.418)		
Day 729 (n= 8, 4)	31.28 (± 15.366)	34.92 (± 11.357)		
Day 785 (n= 4, 4)	11.63 (± 22.691)	40.04 (± 26.752)		
Day 841 (n= 7, 4)	24.27 (± 18.109)	38.54 (± 23.649)		
Day 897 (n= 7, 2)	31.85 (± 17.303)	56.83 (± 20.035)		
Day 953 (n= 6, 0)	23.93 (± 14.964)	999 (± 999)		
Day 1009 (n= 7, 0)	23.99 (± 19.396)	999 (± 999)		
Day 1065 (n= 6, 0)	29.07 (± 17.334)	999 (± 999)		
Day 1121 (n= 7, 0)	27.27 (± 14.536)	999 (± 999)		
Day 1177 (n= 5, 0)	32.28 (± 11.180)	999 (± 999)		
Day 1233 (n= 5, 0)	33.08 (± 10.196)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in free hemoglobin

End point title	Absolute change from baseline in free hemoglobin

End point description:

Free hemoglobin was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan. Baseline is defined as the mean of all pre-dose measurements.

End point type	Secondary

End point timeframe:

Baseline; day 1, 2, 8, 15, 22, 29, 36, 43, 57, 71, 85, 92, 113, 127, 141, 155, 169, 197, 225, 253, 281, 309, 337, 393, 449, 505, 561, 617, 673, 729, 785, 841, 897, 953, 1009, 1065, 1121, 1177, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: mg/dL				
arithmetic mean (standard deviation)				
Day 1 (n= 10, 6)	15.26 (± 36.879)	9.16 (± 15.310)		
Day 2 (n= 10, 6)	-26.73 (± 40.706)	-3.94 (± 6.785)		
Day 8 (n= 9, 6)	-24.03 (± 43.102)	-2.04 (± 6.725)		
Day 15 (n= 10, 6)	-23.16 (± 41.190)	14.21 (± 43.762)		
Day 22 (n= 10, 6)	-22.90 (± 39.726)	-0.66 (± 6.960)		
Day 29 (n= 10, 6)	-20.03 (± 42.349)	-1.21 (± 8.108)		
Day 36 (n= 10, 6)	-12.42 (± 47.495)	-2.56 (± 6.914)		
Day 43 (n= 9, 6)	-13.63 (± 24.961)	-0.54 (± 6.546)		
Day 57 (n= 8, 6)	1.71 (± 14.138)	-1.84 (± 6.662)		
Day 71 (n= 9, 4)	-17.92 (± 34.378)	0.18 (± 1.466)		
Day 85 (n= 10, 4)	-16.80 (± 47.407)	1.90 (± 2.338)		
Day 92 (n= 8, 5)	-25.12 (± 42.237)	-3.31 (± 6.295)		
Day 113 (n= 9, 5)	-24.00 (± 41.084)	16.09 (± 42.454)		
Day 127 (n= 9, 5)	-18.07 (± 52.791)	1.42 (± 2.945)		
Day 141 (n= 10, 5)	-24.03 (± 40.625)	-1.52 (± 8.137)		
Day 155 (n= 9, 4)	-20.58 (± 43.690)	-2.43 (± 8.741)		
Day 169 (n= 9, 5)	-1.00 (± 91.222)	10.24 (± 19.275)		
Day 197 (n= 10, 4)	14.93 (± 105.958)	3.19 (± 5.185)		
Day 225 (n= 10, 3)	10.64 (± 101.866)	15.89 (± 32.159)		
Day 253 (n= 10, 4)	-21.97 (± 40.320)	34.84 (± 61.838)		
Day 281 (n= 10, 5)	-24.19 (± 39.910)	-1.36 (± 7.326)		
Day 309 (n= 10, 4)	-21.57 (± 42.638)	-2.26 (± 9.656)		
Day 337 (n= 10, 3)	-20.69 (± 42.592)	31.39 (± 55.947)		
Day 393 (n= 9, 3)	-17.29 (± 42.263)	-2.11 (± 8.297)		

Day 449 (n= 8, 5)	-28.60 (± 44.210)	-3.93 (± 7.781)		
Day 505 (n= 7, 6)	-33.24 (± 41.787)	-1.69 (± 6.335)		
Day 561 (n= 7, 4)	-34.25 (± 43.692)	1.59 (± 2.372)		
Day 617 (n= 7, 5)	-34.68 (± 44.127)	-0.22 (± 6.960)		
Day 673 (n= 5, 4)	-37.43 (± 54.005)	2.39 (± 15.832)		
Day 729 (n= 8, 4)	-28.88 (± 38.550)	-3.99 (± 7.294)		
Day 785 (n= 4, 2)	-2.55 (± 4.388)	-0.67 (± 3.206)		
Day 841 (n= 7, 4)	-33.12 (± 43.462)	1.60 (± 4.485)		
Day 897 (n= 4, 2)	-12.98 (± 22.233)	4.77 (± 5.468)		
Day 953 (n= 7, 0)	-34.41 (± 46.196)	999 (± 999)		
Day 1009 (n= 7, 0)	8.39 (± 135.082)	999 (± 999)		
Day 1065 (n= 7, 0)	-34.10 (± 44.867)	999 (± 999)		
Day 1121 (n= 7, 0)	-33.45 (± 43.628)	999 (± 999)		
Day 1177 (n= 3, 0)	-16.30 (± 23.441)	999 (± 999)		
Day 1233 (n= 3, 0)	-12.27 (± 20.734)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in reticulocytes count

End point title	Absolute change from baseline in reticulocytes count

End point description:

Reticulocytes count was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan.
Baseline is defined as the mean of all pre-dose measurements.

End point type	Secondary

End point timeframe:

Baseline; day 1, 2, 8, 15, 22, 29, 36, 43, 57, 71, 85, 92, 113, 127, 141, 155, 169, 197, 225, 253, 281, 309, 337, 393, 449, 505, 561, 617, 673, 729, 785, 841, 897, 953, 1009, 1065, 1121, 1177, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: 10^9/L				
arithmetic mean (standard deviation)				
Day 1 (n= 10, 5)	4.44 (± 33.269)	1.62 (± 22.790)		
Day 2 (n= 10, 6)	8.61 (± 52.306)	4.39 (± 31.658)		
Day 8 (n= 10, 6)	-96.94 (± 69.179)	-104.55 (± 88.085)		
Day 15 (n= 10, 6)	-130.15 (± 80.335)	-130.40 (± 107.295)		
Day 22 (n= 10, 6)	-139.26 (± 78.206)	-147.70 (± 99.438)		
Day 29 (n= 10, 6)	-132.28 (± 76.822)	-169.68 (± 129.743)		
Day 36 (n= 10, 6)	-130.73 (± 72.017)	-167.51 (± 137.214)		
Day 43 (n= 10, 6)	-129.02 (± 64.301)	-160.05 (± 132.859)		
Day 57 (n= 10, 6)	-117.69 (± 65.394)	-149.53 (± 116.803)		
Day 71 (n= 8, 4)	-106.83 (± 62.973)	-146.87 (± 129.217)		
Day 85 (n= 10, 3)	-113.96 (± 65.278)	-167.16 (± 156.013)		
Day 92 (n= 10, 5)	-110.54 (± 62.638)	-150.02 (± 105.893)		
Day 113 (n= 9, 5)	-96.78 (± 66.366)	-147.06 (± 129.118)		
Day 127 (n= 9, 4)	-107.84 (± 57.904)	-149.92 (± 115.401)		
Day 141 (n= 10, 5)	-115.17 (± 70.942)	-108.39 (± 54.412)		
Day 155 (n= 8, 5)	-99.90 (± 62.273)	-98.67 (± 65.700)		
Day 169 (n= 10, 5)	-109.39 (± 63.159)	-84.57 (± 64.082)		
Day 197 (n= 10, 3)	-98.87 (± 85.280)	-152.09 (± 137.856)		
Day 225 (n= 10, 3)	-104.11 (± 72.206)	-143.68 (± 149.716)		
Day 253 (n= 10, 4)	-104.30 (± 64.401)	-139.05 (± 127.212)		
Day 281 (n= 9, 4)	-111.11 (± 60.896)	-121.06 (± 66.564)		
Day 309 (n= 9, 4)	-116.88 (± 51.145)	-114.06 (± 77.982)		
Day 337 (n= 9, 4)	-113.31 (± 61.144)	-170.89 (± 142.577)		
Day 393 (n= 9, 4)	-58.54 (± 152.003)	-183.20 (± 122.298)		
Day 449 (n= 8, 5)	-89.44 (± 77.782)	-152.66 (± 124.244)		
Day 505 (n= 7, 6)	-100.68 (± 64.132)	-135.80 (± 117.488)		

Day 561 (n= 6, 5)	-101.63 (± 67.525)	-163.34 (± 121.860)		
Day 617 (n= 7, 6)	-101.73 (± 54.916)	-132.40 (± 122.940)		
Day 673 (n= 5, 5)	-137.05 (± 63.373)	-150.14 (± 130.898)		
Day 729 (n= 8, 4)	-101.16 (± 63.442)	-179.15 (± 131.007)		
Day 785 (n= 4, 4)	-56.22 (± 26.739)	-134.60 (± 141.947)		
Day 841 (n= 7, 4)	-103.96 (± 60.469)	-145.80 (± 140.363)		
Day 897 (n= 7, 2)	-111.41 (± 58.641)	-81.27 (± 36.298)		
Day 953 (n= 5, 0)	-91.00 (± 52.203)	999 (± 999)		
Day 1009 (n= 7, 0)	-110.33 (± 61.354)	999 (± 999)		
Day 1065 (n= 6, 0)	-127.35 (± 61.501)	999 (± 999)		
Day 1121 (n= 7, 0)	-115.96 (± 55.981)	999 (± 999)		
Day 1177 (n= 5, 0)	-140.14 (± 73.898)	999 (± 999)		
Day 1233 (n= 5, 0)	-123.40 (± 70.558)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in C3 fragment deposition on PNH RBC

End point title	Absolute change from baseline in C3 fragment deposition on PNH RBC

End point description:

C3 fragment deposition on PNH Red blood cell (RBC) was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan.
Baseline is defined as Day 1 pre-dose measurement.

End point type	Secondary

End point timeframe:

Day 1 pre dose, day 8, 22, 29, 57, 92, 113, 141, 169, 253, 337, 505, 673, 785, 953, 1121, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	5		
Units: % C3 fragment deposition on PNH RBC				
arithmetic mean (standard deviation)				

Day 8 (n= 10, 5)	-5.59 (± 6.541)	-1.24 (± 4.510)		
Day 22 (n= 8, 4)	-8.02 (± 8.198)	-2.35 (± 5.620)		
Day 29 (n= 8, 5)	-11.64 (± 7.990)	-4.36 (± 2.662)		
Day 57 (n= 8, 3)	-8.90 (± 5.778)	-5.35 (± 2.357)		
Day 92 (n= 7, 3)	-8.70 (± 6.310)	-6.21 (± 0.866)		
Day 113 (n= 7, 2)	-13.65 (± 9.927)	-5.10 (± 2.478)		
Day 141 (n= 6, 2)	-13.18 (± 11.489)	-6.19 (± 4.818)		
Day 169 (n= 7, 2)	-11.06 (± 5.874)	-4.66 (± 3.175)		
Day 253 (n= 9, 4)	-10.08 (± 6.259)	-4.36 (± 1.538)		
Day 337 (n= 7, 2)	-11.21 (± 6.118)	-4.08 (± 3.340)		
Day 505 (n= 3, 4)	-16.04 (± 2.732)	-6.76 (± 2.650)		
Day 673 (n= 4, 0)	-15.19 (± 2.805)	999 (± 999)		
Day 785 (n= 1, 0)	-1.00 (± 999)	999 (± 999)		
Day 953 (n= 2, 0)	-15.28 (± 3.528)	999 (± 999)		
Day 1121 (n= 1, 0)	-0.94 (± 999)	999 (± 999)		
Day 1233 (n= 1, 0)	-12.74 (± 999)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean PNH clone size

End point title	Mean PNH clone size

End point description:

Mean PNH clone size was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan.
Baseline is defined as the mean of all pre-dose measurements.

End point type	Secondary

End point timeframe:

Day 1 pre dose, day 8, 22, 29, 57, 92, 113, 141, 169, 253, 337, 505, 673, 785, 953, 1121, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: PNH Red Blood Cells				
arithmetic mean (standard deviation)				

Day 1 pre dose (n= 10, 5)	54.75 (± 32.536)	46.10 (± 31.436)		
Day 8 (n= 9, 6)	66.32 (± 29.570)	64.45 (± 27.711)		
Day 22 (n= 8, 5)	75.23 (± 23.458)	79.37 (± 20.270)		
Day 29 (n= 8, 6)	75.34 (± 20.837)	78.87 (± 17.642)		
Day 57 (n= 9, 5)	85.87 (± 15.660)	86.45 (± 12.576)		
Day 92 (n= 8, 5)	89.20 (± 16.861)	85.38 (± 12.939)		
Day 113 (n= 8, 3)	89.28 (± 18.936)	86.02 (± 9.626)		
Day 141 (n= 8, 3)	93.91 (± 6.105)	80.25 (± 6.638)		
Day 169 (n= 8, 3)	87.60 (± 19.644)	83.69 (± 11.187)		
Day 253 (n= 9, 4)	90.30 (± 18.176)	82.28 (± 12.649)		
Day 337 (n= 8, 3)	88.69 (± 20.381)	91.68 (± 11.905)		
Day 505 (n= 3, 5)	98.33 (± 1.738)	88.45 (± 10.419)		
Day 673 (n= 4, 2)	97.45 (± 2.370)	92.48 (± 6.626)		
Day 785 (n= 2, 0)	83.61 (± 9.327)	999 (± 999)		
Day 953 (n= 2, 0)	96.08 (± 3.825)	999 (± 999)		
Day 1121 (n= 2, 0)	93.74 (± 7.410)	999 (± 999)		
Day 1233 (n= 3, 0)	69.83 (± 43.045)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Haptoglobin levels

End point title	Mean Haptoglobin levels

End point description:

Haptoglobin level was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan. Baseline is defined as the mean of all pre-dose measurements.

End point type	Secondary

End point timeframe:

Day 2, 8, 15, 22, 29, 36, 43, 57, 71, 85, 92, 113, 127, 141, 155, 169, 197, 225, 253, 281, 309, 337, 393, 449, 505, 561, 617, 673, 729, 785, 841, 897, 953, 1009, 1065, 1121, 1177, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	4		
Units: g/L				
arithmetic mean (standard deviation)				
Day 2 (n= 2, 2)	0.55 (± 0.071)	0.30 (± 0.141)		
Day 8 (n= 7, 3)	0.70 (± 0.548)	0.77 (± 0.306)		
Day 15 (n= 9, 2)	0.93 (± 0.960)	0.60 (± 0.141)		
Day 22 (n= 8, 4)	1.18 (± 1.387)	0.70 (± 0.483)		
Day 29 (n= 7, 3)	0.94 (± 0.896)	0.83 (± 0.586)		
Day 36 (n= 5, 3)	1.08 (± 0.779)	0.97 (± 0.503)		
Day 43 (n= 5, 3)	1.26 (± 1.401)	0.70 (± 0.520)		
Day 57 (n= 3, 1)	0.63 (± 0.416)	1.20 (± 999)		
Day 71 (n= 4, 1)	0.75 (± 0.473)	0.80 (± 999)		
Day 85 (n= 3, 0)	0.87 (± 0.611)	999 (± 999)		
Day 92 (n= 2, 1)	0.95 (± 0.495)	0.80 (± 999)		
Day 113 (n= 3, 1)	0.63 (± 0.493)	0.50 (± 999)		
Day 127 (n= 3, 0)	0.47 (± 0.208)	999 (± 999)		
Day 141 (n= 3, 1)	0.57 (± 0.306)	0.70 (± 999)		
Day 155 (n= 1, 1)	0.50 (± 999)	0.80 (± 999)		
Day 169 (n= 3, 1)	0.63 (± 0.577)	0.50 (± 999)		
Day 197 (n= 3, 0)	0.80 (± 0.700)	999 (± 999)		
Day 225 (n= 4, 0)	0.65 (± 0.705)	999 (± 999)		
Day 253 (n= 4, 0)	0.63 (± 0.519)	999 (± 999)		
Day 281 (n= 2, 1)	0.50 (± 0.283)	0.30 (± 999)		
Day 309 (n= 2, 1)	0.75 (± 0.071)	0.50 (± 999)		
Day 337 (n= 1, 0)	0.40 (± 999)	999 (± 999)		
Day 393 (n= 2, 0)	0.60 (± 0.283)	999 (± 999)		
Day 449 (n= 1, 1)	0.20 (± 999)	0.60 (± 999)		
Day 505 (n= 2, 1)	0.60 (± 0.141)	0.60 (± 999)		
Day 561 (n= 1, 1)	0.60 (± 999)	0.70 (± 999)		
Day 617 (n= 2, 2)	0.30 (± 0.141)	1.90 (± 1.838)		
Day 673 (n= 1, 1)	0.30 (± 999)	0.70 (± 999)		
Day 729 (n= 2, 1)	0.35 (± 0.071)	0.50 (± 999)		
Day 785 (n= 1, 2)	1.00 (± 999)	1.25 (± 0.919)		
Day 841 (n= 3, 2)	0.47 (± 0.153)	0.85 (± 0.212)		
Day 897 (n= 3, 0)	0.33 (± 0.058)	999 (± 999)		
Day 953 (n= 2, 0)	0.50 (± 0.141)	999 (± 999)		
Day 1009 (n= 2, 0)	0.45 (± 0.071)	999 (± 999)		
Day 1065 (n= 2, 0)	2.05 (± 1.768)	999 (± 999)		
Day 1121 (n= 4, 0)	1.00 (± 0.935)	999 (± 999)		
Day 1177 (n= 2, 0)	0.40 (± 0.000)	999 (± 999)		
Day 1233 (n= 2, 0)	0.95 (± 0.636)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in total bilirubin

End point title	Absolute change from baseline in total bilirubin

End point description:

Bilirubin was used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan.
Baseline is defined as the mean of all pre-dose measurements.

End point type	Secondary

End point timeframe:

Baseline; day 1, 2, 8, 15, 22, 29, 36, 43, 57, 71, 85, 92, 113, 127, 141, 155, 169, 197, 225, 253, 281, 309, 337, 393, 449, 505, 561, 617, 673, 729, 785, 841, 897, 953, 1009, 1065, 1121, 1177, 1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: umol/L				
arithmetic mean (standard deviation)				
Day 1 (n= 10, 6)	2.94 (± 13.038)	1.36 (± 4.978)		
Day 2 (n= 10, 6)	-21.06 (± 15.647)	-25.47 (± 21.598)		
Day 8 (n= 10, 6)	-23.66 (± 16.081)	-25.97 (± 24.380)		
Day 15 (n= 10, 6)	-23.86 (± 16.538)	-26.97 (± 24.043)		
Day 22 (n= 10, 6)	-25.36 (± 15.403)	-25.14 (± 23.541)		
Day 29 (n= 10, 6)	-24.66 (± 15.026)	-26.14 (± 22.345)		
Day 36 (n= 10, 6)	-23.96 (± 15.945)	-25.31 (± 27.658)		
Day 43 (n= 10, 6)	-24.66 (± 14.552)	-25.14 (± 23.727)		
Day 57 (n= 10, 6)	-24.16 (± 13.946)	-22.81 (± 21.233)		
Day 71 (n= 10, 4)	-23.16 (± 15.154)	-27.92 (± 24.924)		
Day 85 (n= 10, 4)	-23.66 (± 14.595)	-28.42 (± 26.075)		
Day 92 (n= 10, 5)	-21.66 (± 13.985)	-27.87 (± 25.234)		
Day 113 (n= 9, 5)	-21.06 (± 15.026)	-26.87 (± 23.200)		
Day 127 (n= 9, 4)	-22.18 (± 13.357)	-27.79 (± 26.965)		
Day 141 (n= 10, 5)	-22.46 (± 14.404)	-18.23 (± 9.473)		
Day 155 (n= 9, 5)	-19.73 (± 12.376)	-16.23 (± 9.565)		
Day 169 (n= 10, 5)	-21.66 (± 13.383)	-14.83 (± 10.281)		

Day 197 (n= 9, 4)	-24.21 (± 13.678)	-23.71 (± 28.849)		
Day 225 (n= 10, 3)	-23.06 (± 12.410)	-30.06 (± 36.183)		
Day 253 (n= 10, 4)	-21.36 (± 12.192)	-24.21 (± 30.342)		
Day 281 (n= 10, 4)	-23.46 (± 12.150)	-16.54 (± 8.694)		
Day 309 (n= 10, 4)	-22.86 (± 12.078)	-11.21 (± 10.635)		
Day 337 (n= 10, 4)	-22.76 (± 13.248)	-28.71 (± 29.338)		
Day 393 (n= 9, 4)	-19.73 (± 15.644)	-28.00 (± 27.769)		
Day 449 (n= 8, 5)	-24.64 (± 13.021)	-23.50 (± 25.603)		
Day 505 (n= 7, 6)	-27.30 (± 12.450)	-25.81 (± 24.978)		
Day 561 (n= 7, 5)	-21.98 (± 14.718)	-21.10 (± 30.888)		
Day 617 (n= 6, 6)	-28.85 (± 11.516)	-23.47 (± 21.451)		
Day 673 (n= 5, 5)	-27.58 (± 13.453)	-24.50 (± 25.562)		
Day 729 (n= 8, 4)	-23.64 (± 12.971)	-32.13 (± 28.799)		
Day 785 (n= 4, 4)	-11.54 (± 5.370)	-26.67 (± 33.656)		
Day 841 (n= 7, 4)	-20.49 (± 12.006)	-29.42 (± 32.316)		
Day 897 (n= 7, 2)	-24.49 (± 13.627)	-16.00 (± 7.542)		
Day 953 (n= 7, 0)	-23.92 (± 14.707)	999 (± 999)		
Day 1009 (n= 7, 0)	-23.92 (± 14.204)	999 (± 999)		
Day 1065 (n= 6, 0)	-25.65 (± 13.844)	999 (± 999)		
Day 1121 (n= 7, 0)	-23.35 (± 14.363)	999 (± 999)		
Day 1177 (n= 5, 0)	-29.78 (± 11.559)	999 (± 999)		
Day 1233 (n= 5, 0)	-28.78 (± 12.328)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics profile: Maximum plasma concentration (Cmax)

End point title	Pharmacokinetics profile: Maximum plasma concentration (Cmax)[2]

End point description:

Cmax is the maximum (peak) observed plasma drug concentration after single dose administration (mass x volume-1).
PK assessment parameters were determined using the actual recorded sampling times and non-compartmental methods.
In Cohort 2, patients were supposed to be orally administered iptacopan 50 mg b.i.d. in addition to SoC;

this was increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values. One patient in Cohort 2 was orally administered iptacopan 25 mg at day 1 due to a dosing error.
No statistical analysis was planned for this outcome.

End point type	Secondary

End point timeframe:

Day 1, 29, 169, 337

Notes:

[2] - 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	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 25mg bid + SoC	Cohort 2: LNP023 50mg bid + SoC	Cohort 2: LNP023 200mg bid + SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	1	6	3
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 (n= 10, 1, 5, 0)	3400 (± 1060)	1610 (± 999)	1570 (± 366)	999 (± 999)
Day 29 (n= 10, 0, 6, 0)	3500 (± 1340)	999 (± 999)	1770 (± 469)	999 (± 999)
Day 169 (n= 9, 0, 1, 3)	3530 (± 853)	999 (± 999)	1180 (± 999)	3130 (± 824)
Day 337 (n= 9, 0, 1, 3)	4030 (± 1140)	999 (± 999)	2470 (± 999)	4370 (± 1790)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with on study transfusions from packed RBC units

End point title	Number of participants with on study transfusions from packed RBC units

End point description:

Number of participants with on study transfusions from packed RBC units was collected.

End point type	Secondary

End point timeframe:

Up to 46 months

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: Participants	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics profile: Area Under the Curve (AUC) tau

End point title	Pharmacokinetics profile: Area Under the Curve (AUC) tau[3]

End point description:

The AUCtau is the area under the plasma concentration-time curve calculated to the end of a dosing interval (tau) at steady-state.
PK assessment parameters were determined using the actual recorded sampling times and non-compartmental methods.
In Cohort 2, patients were supposed to be orally administered iptacopan 50 mg b.i.d. in addition to SoC; this was increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values. One patient in Cohort 2 was orally administered iptacopan 25 mg at day 1 due to a dosing error.
No statistical analysis was planned for this outcome.

End point type	Secondary

End point timeframe:

day 1, 29, 169, 337

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	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 25mg bid + SoC	Cohort 2: LNP023 50mg bid + SoC	Cohort 2: LNP023 200mg bid + SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	1	6	3
Units: h*ng/mL				
arithmetic mean (standard deviation)				
Day 1 (n= 10, 1, 5, 0)	18200 (± 6700)	9470 (± 999)	8620 (± 1310)	999 (± 999)
Day 29 (n= 10, 0, 6, 0)	24400 (± 8720)	999 (± 999)	14800 (± 4100)	999 (± 999)
Day 169 (n= 9, 0, 1, 3)	25600 (± 7570)	999 (± 999)	10700 (± 999)	23900 (± 5920)
Day 337 (n= 9, 0, 1, 3)	26900 (± 7640)	999 (± 999)	16900 (± 999)	37800 (± 15500)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics profile: Time to reach maximum plasma concentration (Tmax)

End point title	Pharmacokinetics profile: Time to reach maximum plasma concentration (Tmax)[4]

End point description:

Tmax is the time to reach maximum (peak) plasma drug concentration after single dose administration (time).
PK assessment parameters were determined using the actual recorded sampling times and non-compartmental methods.
In Cohort 2, patients were supposed to be orally administered iptacopan 50 mg b.i.d. in addition to SoC; this was increased to iptacopan 200 mg b.i.d. at study day 15 or at any time later in the study if LDH was not within limit of normal or reduced by at least 60% as compared to baseline values. One patient

in Cohort 2 was orally administered iptacopan 25 mg at day 1 due to a dosing error.
No statistical analysis was planned for this outcome.

End point type	Secondary

End point timeframe:

Day 1, 29, 169, 337

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	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 25mg bid + SoC	Cohort 2: LNP023 50mg bid + SoC	Cohort 2: LNP023 200mg bid + SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	1	6	3
Units: hours				
median (full range (min-max))				
Day 1 (n= 10, 1, 5, 0)	1.50 (1.00 to 6.00)	2.00 (2.00 to 2.00)	2.00 (2.00 to 2.00)	999 (999 to 999)
Day 29 (n= 10, 0, 6, 0)	2.00 (1.00 to 2.00)	999 (999 to 999)	2.04 (2.00 to 4.00)	999 (999 to 999)
Day 169 (n= 9, 0, 1, 3)	2.00 (1.00 to 4.00)	999 (999 to 999)	4.00 (4.00 to 4.00)	2.00 (1.83 to 2.00)
Day 337 (n= 9, 0, 1, 3)	2.00 (1.00 to 2.00)	999 (999 to 999)	2.03 (2.03 to 2.03)	2.00 (1.05 to 5.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Red Blood Cell Count: Mean erythrocytes levels

End point title	Red Blood Cell Count: Mean erythrocytes levels

End point description:

Erythrocytes levels were used as a marker of intra and extravascular hemolysis when administered in addition to SoC (monoclonal antibody with anti C5 activity) to assess the effect of iptacopan.

End point type	Secondary

End point timeframe:

Screening, Baseline, Day 2,8,15,22,29,36,43,57,71,85,92,113,127,141,155,169,197,225,253,281,309,337,393,449,505,561,617,673,729,729,785,841,897,953,1009,1065,1121,1177,1233

End point values	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 50mg/200mg bid + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: 10^12/L				
arithmetic mean (standard deviation)				
Screening (n = 9, 5)	3.12 (± 0.887)	2.42 (± 0.427)		
Baseline (n = 9, 5)	2.73 (± 0.466)	2.40 (± 0.442)		

Day 1 (n = 10, 5)	2.67 (± 0.615)	2.16 (± 0.498)		
Day 2 (n = 10, 6)	2.70 (± 0.485)	2.17 (± 0.520)		
Day 8 (n = 10, 6)	3.17 (± 0.585)	3.00 (± 0.812)		
Day 15 (n = 10, 6)	3.43 (± 0.723)	3.23 (± 0.794)		
Day 22 (n = 10, 6)	3.58 (± 0.835)	3.57 (± 0.900)		
Day 29 (n = 10, 6)	3.72 (± 0.857)	3.62 (± 0.870)		
Day 36 (n = 10, 6)	3.75 (± 0.753)	3.62 (± 0.804)		
Day 43 (n = 10, 6)	3.67 (± 0.807)	3.55 (± 0.758)		
Day 57 (n = 10, 6)	3.69 (± 0.852)	3.72 (± 0.574)		
Day 71 (n = 8, 4)	3.50 (± 0.787)	3.48 (± 0.591)		
Day 85 (n = 10, 3)	3.65 (± 0.841)	3.60 (± 0.520)		
Day 92 (n = 10, 5)	3.76 (± 0.828)	3.56 (± 0.483)		
Day 113 (n = 9, 5)	3.58 (± 0.807)	3.58 (± 0.444)		
Day 127 (n = 9, 4)	3.69 (± 0.822)	3.75 (± 0.265)		
Day 141 (n = 10, 5)	3.64 (± 0.799)	3.44 (± 0.493)		
Day 155 (n = 8, 5)	3.53 (± 0.815)	3.52 (± 0.432)		
Day 169 (n = 10, 5)	3.62 (± 0.826)	3.54 (± 0.378)		
Day 197 (n = 10, 3)	3.68 (± 0.774)	3.77 (± 0.577)		
Day 225 (n = 10, 3)	3.70 (± 0.894)	3.43 (± 0.513)		
Day 253 (n = 10, 4)	3.62 (± 0.930)	3.45 (± 0.412)		
Day 281 (n = 9, 4)	3.81 (± 0.875)	3.73 (± 0.403)		
Day 309 (n = 9, 4)	3.50 (± 0.728)	3.58 (± 0.427)		
Day 337 (n = 9, 4)	3.50 (± 0.714)	3.75 (± 0.580)		
Day 393 (n = 9, 4)	3.63 (± 0.876)	4.00 (± 0.356)		
Day 449 (n = 8, 5)	3.80 (± 0.920)	3.94 (± 0.378)		
Day 505 (n = 7, 6)	3.63 (± 1.053)	3.92 (± 0.360)		
Day 561 (n = 6, 5)	3.47 (± 0.937)	3.92 (± 0.370)		
Day 617 (n = 7, 6)	3.80 (± 1.149)	3.85 (± 0.389)		
Day 673 (n =5, 5)	3.74 (± 0.716)	3.86 (± 0.270)		
Day 729 (n = 8, 4)	3.74 (± 1.021)	3.93 (± 0.150)		
Day 785 (n = 4, 4)	2.83 (± 0.618)	3.78 (± 0.263)		
Day 841 (n = 7, 4)	3.64 (± 1.081)	3.80 (± 0.294)		
Day 897 (n = 7, 2)	3.89 (± 1.123)	3.95 (± 0.071)		
Day 953 (n = 6, 0)	3.62 (± 1.196)	999 (± 999)		
Day 1009 (n = 7, 0)	3.61 (± 1.316)	999 (± 999)		
Day 1065 (n = 6, 0)	3.87 (± 1.073)	999 (± 999)		
Day 1121 (n = 7, 0)	3.69 (± 1.006)	999 (± 999)		
Day 1177 (n = 5, 0)	4.06 (± 0.829)	999 (± 999)		
Day 1233 (n = 5, 0)	4.14 (± 0.844)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

AEs were reported from first dose of study treatment until EoS treatment plus 14 days post treatment. SAEs were reported from first dose of study treatment until EoS treatment plus 30 days post treatment, up to a maximum duration of 189 weeks.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Cohort 1: LNP023 200mg bid + SoC

Reporting group description:

Orally administered iptacopan 200 mg b.i.d. in Part 1 and Part 2 in addition to SoC.

Reporting group title	Cohort 2: LNP023 200mg bid + SoC

Reporting group description:

Orally administered iptacopan 50 mg b.i.d. in Part 1 and iptacopan 50 mg b.i.d. or 200 mg b.i.d. in Part 2 in addition to SoC.
This arm summarizes all events that started when treated with iptacopan 200 mg b.i.d. in Cohort 2.
Total number at risk only includes patients who received LNP023 200mg bid.

Reporting group title	Total

Reporting group description:

Total

Reporting group title	Cohort 2: LNP023 50mg bid + SoC

Reporting group description:

Orally administered iptacopan 50 mg b.i.d. in Part 1 and iptacopan 50 mg b.i.d. or 200 mg b.i.d. in Part 2 in addition to SoC.
This arm summarizes all events that started when treated with iptacopan 50 mg b.i.d. in Cophort 2

Serious adverse events	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 200mg bid + SoC	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	2 / 5 (40.00%)	6 / 16 (37.50%)
number of deaths (all causes)	3	0	3
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoproliferative disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Penetrating aortic ulcer			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary bladder polyp			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2: LNP023 50mg bid + SoC		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphoproliferative disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the tongue			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Penetrating aortic ulcer			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary bladder polyp			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: LNP023 200mg bid + SoC	Cohort 2: LNP023 200mg bid + SoC	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	5 / 5 (100.00%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Angiofibroma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Haematoma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Hot flush			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
Medical device site pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Medical device site irritation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Asthenia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	4 / 16 (25.00%)
occurrences (all)	5	0	7
Non-cardiac chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Pyrexia			

subjects affected / exposed	3 / 10 (30.00%)	1 / 5 (20.00%)	5 / 16 (31.25%)
occurrences (all)	4	1	8
Social circumstances			
Andropause			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Genital discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Dysmenorrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	2
Breast pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Vulvovaginal dryness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Haematospermia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Rhinorrhoea			

subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	3 / 16 (18.75%)
occurrences (all)	2	0	3
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	3 / 16 (18.75%)
occurrences (all)	2	0	3
Nightmare			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Poor quality sleep			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Investigations			
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Foot fracture			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	2
Contusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Traumatic haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vaccination complication			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	2	3
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	2 / 10 (20.00%)	1 / 5 (20.00%)	5 / 16 (31.25%)
occurrences (all)	2	1	5
Migraine			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Anosmia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ageusia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sciatica			

subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 5 (20.00%)	3 / 16 (18.75%)
occurrences (all)	4	1	5
Thrombocytopenia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 5 (20.00%)	3 / 16 (18.75%)
occurrences (all)	2	1	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Aphthous ulcer			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	2
Dysphagia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	3
Tongue ulceration			

subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Hepatobiliary disorders			
Ocular icterus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Hepatic cytolysis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Alopecia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Ecchymosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Dry skin			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Dermatitis acneiform			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Eczema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Onycholysis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Petechiae			

subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	1 / 5 (20.00%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Psoriasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	2 / 5 (40.00%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Nocturia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Pollakiuria			
subjects affected / exposed	1 / 10 (10.00%)	1 / 5 (20.00%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Dysuria			
subjects affected / exposed	2 / 10 (20.00%)	1 / 5 (20.00%)	3 / 16 (18.75%)
occurrences (all)	4	1	5
Urinary bladder polyp			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Osteopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Joint swelling			

subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Chondropathy			
subjects affected / exposed	0 / 10 (0.00%)	2 / 5 (40.00%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Back pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	2
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Spinal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	2
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	2
Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	3
Pyelonephritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 5 (20.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

Periodontitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Oral herpes			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Fungal skin infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Herpes zoster			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	4	0	4
Rhinitis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	2 / 16 (12.50%)
occurrences (all)	4	0	4
Wound infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vaginal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Hypertriglyceridaemia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 5 (0.00%)	4 / 16 (25.00%)
occurrences (all)	2	0	4
Hyperferritinaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Hypercholesterolaemia			

subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Vitamin B12 deficiency			
subjects affected / exposed	1 / 10 (10.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1

Non-serious adverse events	Cohort 2: LNP023 50mg bid + SoC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiofibroma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Medical device site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Medical device site irritation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Asthenia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 3		
Social circumstances Andropause subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Reproductive system and breast disorders Genital discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Breast pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Vulvovaginal dryness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Haematospermia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		

Cough subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Upper respiratory tract congestion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Epistaxis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Psychiatric disorders Alcohol abuse subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Insomnia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Nightmare subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Poor quality sleep subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Investigations SARS-CoV-2 test negative subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Traumatic haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vaccination complication			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Paraesthesia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Anosmia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Ageusia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aphthous ulcer			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphagia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Tongue ulceration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hepatobiliary disorders			
Ocular icterus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatic cytolysis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Onycholysis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Petechiae subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Psoriasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nocturia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pollakiuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dysuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Urinary bladder polyp subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Endocrine disorders Hyperthyroidism			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Osteopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chondropathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Periodontitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fungal skin infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Wound infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vaginal infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			

Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Hyperferritinaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2017	Eligibility criteria updated to exclude patients with hepatitis. Study stopping rules updated to state that the occurrence of one or more fatal or life-threatening severe reactions, considered by the Investigator as potentially related to iptacopan, would trigger a pause of enrollment and dosing of affected patient(s). Details on physical examination and SAE reporting (previously only available in Site Operations Manual) were added.
23 January 2018	Detail of DMC and DMC's involvement in decisions regarding potential study stopping added
24 July 2018	Treatment duration prolonged beyond 13 weeks and up to 12 months for PNH patients enrolled in this study who have shown clinical benefits from iptacopan treatment. Upper limit of age was updated from 75 to 80 years old to facilitate recruitment.
01 February 2019	Treatment duration prolonged from approximately 1 year to 3 years. Detail on implementation of a down titration period and guidance for Investigators on how to monitor patients who discontinued iptacopan study treatment added. Detail on the implementation of Cohort 2 where the iptacopan start dose will be lowered to 50 mg b.i.d. with an option to up-titrate the dose to a maximum of 200 mg b.i.d. (original dose), in cases of persistent hemolysis, was added. Eligibility criteria updated to include Cohort 2 patients with LDH levels 1.25 × ULN, but in combination with a reduced hemoglobin level as another inclusion criterion. Detail on permitted eculizumab dose adjustment for stable patients without signs of active hemolysis who are at least for 6 months in the study and having received continued concomitant treatment with iptacopan and eculizumab added. Study endpoints were updated to include PNH-type RBCs and CH50
26 July 2021	Details on option to complete this phase 2 study after a minimum of 2 years of treatment and transition to the REP added (such patients no longer need to complete tapering down period) New wording added to describe Public Health Emergency (pandemic, epidemic or natural disaster) mitigation procedures to ensure patient safety and study integrity

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: