



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of the Safety and Efficacy of OMS721 in Patients with Immunoglobulin A (IgA) Nephropathy (ARTEMIS – IGAN)

Summary

EudraCT number	2018-000075-33
Trial protocol	HU CZ SK LT SE ES BE AT PL BG GB DE IT GR
Global end of trial date	12 January 2024

Results information

Result version number	v1 (current)
This version publication date	14 March 2025
First version publication date	14 March 2025

Trial information

Trial identification

Sponsor protocol code	OMS721-IGA-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03608033
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Omeros Corporation
Sponsor organisation address	201 Elliott Avenue West Seattle, Washington, United States, 98119
Public contact	Amar Sethi, MD, PhD, Omeros, 206 676-5000,
Scientific contact	Amar Sethi, MD, PhD, Omeros, 206 676-5000,

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	12 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 January 2024
Global end of trial reached?	Yes
Global end of trial date	12 January 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the effect of narsoplimab on 24-hour urine protein excretion (UPE) in IgA nephropathy (IgAN) patients with high baseline proteinuria (high-risk proteinuria group; 24-hour UPE ≥ 2 g/day) assessed at 36 weeks from baseline.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice (GCP), according to the International Council on Harmonisation (ICH) Harmonised Tripartite Guideline, and in accordance with 21 CFR 312.120.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 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	Argentina: 2
Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czechia: 12
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	India: 17
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Korea, Republic of: 49
Country: Number of subjects enrolled	Lithuania: 14
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Slovakia: 13
Country: Number of subjects enrolled	Thailand: 11

Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	Türkiye: 12
Country: Number of subjects enrolled	United States: 88
Worldwide total number of subjects	360
EEA total number of subjects	132

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)	345
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted globally at different sites between 05 Apr 2018 and 12 Jan 2024.

Pre-assignment

Screening details:

Overall, 360 subjects were enrolled and randomized into two arms of the study.

Period 1

Period 1 title	87Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Narsoplimab

Arm description:

Subjects received narsoplimab 370 milligram (mg) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30 percent (%) from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period). Subjects with 24-hour UPE >2 g at baseline received open-label narsoplimab at Week 72 once weekly for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Narsoplimab
Investigational medicinal product code	OMS721
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received narsoplimab 370 mg intravenously once per week.

Arm title	Placebo
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Arm description:

Subjects received placebo (vehicle) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30% from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period).

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

Dosage and administration details:

Subject received placebo (vehicle) once per week.

Number of subjects in period 1	Narsoplimab	Placebo
Started	181	179
Received extended treatment	132	129
Received relapse treatment	75	68
Received open label treatment	13 ^[1]	21 ^[2]
Completed	37	39
Not completed	144	140
Physician decision	6	10
Consent withdrawn by subject	46	45
Adverse event, non-fatal	1	5
Protocol violation	1	2
Death	-	1
Pregnancy	1	-
Lost to follow-up	2	6
Site terminated by Sponsor	1	-
Lack of efficacy	4	3
Study terminated by the Sponsor	82	68

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who received treatment in specified period.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who received treatment in specified period.

Baseline characteristics

Reporting groups

Reporting group title	Narsoplimab
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Reporting group description:

Subjects received narsoplimab 370 milligram (mg) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30 percent (%) from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period). Subjects with 24-hour UPE >2 g at baseline received open-label narsoplimab at Week 72 once weekly for 12 weeks.

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo (vehicle) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30% from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period).

Reporting group values	Narsoplimab	Placebo	Total
Number of subjects	181	179	360
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	40.7	41.6	
standard deviation	± 12.01	± 12.76	-
Gender categorical			
Units: Subjects			
Female	67	61	128
Male	114	118	232

End points

End points reporting groups

Reporting group title	Narsoplimab
Reporting group description:	
Subjects received narsoplimab 370 milligram (mg) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30 percent (%) from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period). Subjects with 24-hour UPE >2 g at baseline received open-label narsoplimab at Week 72 once weekly for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo (vehicle) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30% from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period).	

Primary: Percent Change From Baseline in 24-hour Urine Protein Excretion (UPE, 24-hour UPE ≥ 2 g/day) at Week 36

End point title	Percent Change From Baseline in 24-hour Urine Protein Excretion (UPE, 24-hour UPE ≥ 2 g/day) at Week 36
End point description:	
Urine protein was assessed by urinary protein excretion during a 24-hour urine collection. Here "number of subjects analyzed" signifies subjects evaluable for this endpoint. The primary efficacy analysis population was the Full Analysis Set (FAS) population, defined as all randomized subjects in the high-risk proteinuria group (24-hour UPE ≥ 2 g/day).	
End point type	Primary
End point timeframe:	
Baseline, at Week 36	

End point values	Narsoplimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70 ^[1]	69 ^[2]		
Units: percent change				
least squares mean (standard error)	-21.3 (\pm 0.0672)	-16.6 (\pm 0.0680)		

Notes:

[1] - Primary analysis population with evaluable subjects for this end point.

[2] - Primary analysis population with evaluable subjects for this end point.

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Narsoplimab v Placebo

Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5447
Method	t-test, 2-sided
Parameter estimate	Difference in % Change LS Means
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.6
upper limit	13.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the signing informed consent form to end of follow up (Week 96)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Blinded Phase: Narsoplimab
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Reporting group description:

Subjects received narsoplimab 370 mg intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30 percent (%) from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period). Subjects with 24-hour UPE >2 g at baseline received open-label narsoplimab at Week 72 once weekly for 12 weeks.

Reporting group title	Blinded Phase: Placebo
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Reporting group description:

Subjects received placebo (vehicle) intravenously once weekly for 12 weeks during the initial treatment period. Subjects who had a 24-hour UPE >1 g at Week 12, received 6 additional weeks of treatment (extended treatment). Subjects who initially showed a response to treatment of at least 30% from baseline proteinuria at any assessment timepoint but subsequently relapsed (defined as an increase in 24-hour UPE by $\geq 30\%$ from the value of their lowest measured post-treatment UPE and 24-hour UPE >1 g) were retreated once only at Week 24, Week 30, or Week 36. Subjects who relapsed on or after Week 48 were retreated with 12 weekly treatments (administered once in a 12-month period).

Reporting group title	Open Label: Narsoplimab
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Reporting group description:

Subjects with 24-hour UPE >2 g at baseline received open-label narsoplimab 370 mg intravenously at Week 72 once weekly for 12 weeks (if specific requirements were met).

Serious adverse events	Blinded Phase: Narsoplimab	Blinded Phase: Placebo	Open Label: Narsoplimab
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 181 (12.15%)	20 / 179 (11.17%)	7 / 34 (20.59%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nasopharyngeal cancer metastatic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngeal tumour			

subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer metastatic			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm recurrence			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pre-eclampsia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Catheter site haemorrhage			

subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anti-neutrophil cytoplasmic antibody positive vasculitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			

subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haematoma			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			

subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain stem haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 181 (0.55%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Middle ear effusion			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 181 (0.00%)	0 / 179 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 181 (0.00%)	0 / 179 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 181 (1.10%)	3 / 179 (1.68%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			

subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	4 / 181 (2.21%)	1 / 179 (0.56%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	1 / 181 (0.55%)	3 / 179 (1.68%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			
subjects affected / exposed	0 / 181 (0.00%)	0 / 179 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			

subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial disorder			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 181 (0.00%)	2 / 179 (1.12%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye infection toxoplasmal			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			

subjects affected / exposed	0 / 181 (0.00%)	0 / 179 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 179 (0.56%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis externa			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 181 (0.55%)	0 / 179 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 181 (0.55%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 179 (0.56%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Blinded Phase: Narsoplimab	Blinded Phase: Placebo	Open Label: Narsoplimab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	135 / 181 (74.59%)	116 / 179 (64.80%)	24 / 34 (70.59%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 181 (0.00%)	6 / 179 (3.35%)	0 / 34 (0.00%)
occurrences (all)	0	6	0
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 181 (7.73%)	17 / 179 (9.50%)	3 / 34 (8.82%)
occurrences (all)	14	17	3
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 181 (11.05%)	17 / 179 (9.50%)	0 / 34 (0.00%)
occurrences (all)	20	17	0
Dizziness			
subjects affected / exposed	7 / 181 (3.87%)	8 / 179 (4.47%)	0 / 34 (0.00%)
occurrences (all)	7	8	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 181 (4.42%)	6 / 179 (3.35%)	1 / 34 (2.94%)
occurrences (all)	8	6	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 181 (6.63%)	11 / 179 (6.15%)	1 / 34 (2.94%)
occurrences (all)	12	11	1
Oedema peripheral			
subjects affected / exposed	10 / 181 (5.52%)	11 / 179 (6.15%)	0 / 34 (0.00%)
occurrences (all)	10	11	4
Pyrexia			
subjects affected / exposed	10 / 181 (5.52%)	5 / 179 (2.79%)	0 / 34 (0.00%)
occurrences (all)	10	5	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	10 / 181 (5.52%)	10 / 179 (5.59%)	1 / 34 (2.94%)
occurrences (all)	10	10	1
Diarrhoea			

subjects affected / exposed occurrences (all)	8 / 181 (4.42%) 8	8 / 179 (4.47%) 8	1 / 34 (2.94%) 1
Abdominal pain subjects affected / exposed occurrences (all)	6 / 181 (3.31%) 6	5 / 179 (2.79%) 5	0 / 34 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	2 / 181 (1.10%) 2	7 / 179 (3.91%) 7	0 / 34 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	9 / 181 (4.97%) 9	7 / 179 (3.91%) 7	0 / 34 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	7 / 181 (3.87%) 7	5 / 179 (2.79%) 5	1 / 34 (2.94%) 1
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 181 (0.55%) 1	5 / 179 (2.79%) 5	8 / 34 (23.53%) 8
Rash subjects affected / exposed occurrences (all)	3 / 181 (1.66%) 3	7 / 179 (3.91%) 7	1 / 34 (2.94%) 1
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	7 / 181 (3.87%) 7	6 / 179 (3.35%) 6	0 / 34 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	17 / 181 (9.39%) 17	9 / 179 (5.03%) 9	0 / 34 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	10 / 181 (5.52%) 10	8 / 179 (4.47%) 8	1 / 34 (2.94%) 1
Pain in extremity subjects affected / exposed occurrences (all)	7 / 181 (3.87%) 7	2 / 179 (1.12%) 2	1 / 34 (2.94%) 1

Flank pain subjects affected / exposed occurrences (all)	6 / 181 (3.31%) 6	2 / 179 (1.12%) 2	1 / 34 (2.94%) 1
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	44 / 181 (24.31%) 44	38 / 179 (21.23%) 38	3 / 34 (8.82%) 3
Upper respiratory tract infection subjects affected / exposed occurrences (all)	12 / 181 (6.63%) 12	12 / 179 (6.70%) 12	1 / 34 (2.94%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	11 / 181 (6.08%) 11	8 / 179 (4.47%) 8	2 / 34 (5.88%) 2
Viral infection subjects affected / exposed occurrences (all)	0 / 181 (0.00%) 0	2 / 179 (1.12%) 2	2 / 34 (5.88%) 2
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	11 / 181 (6.08%) 11	4 / 179 (2.23%) 4	1 / 34 (2.94%) 1
Gout subjects affected / exposed occurrences (all)	6 / 181 (3.31%) 6	6 / 179 (3.35%) 6	1 / 34 (2.94%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2019	<p>Amendment#1 Continued...</p> <ul style="list-style-type: none">- Added an open-label option for high-risk patients starting 18 months after randomization.- Modification of the inclusion criteria to show that proteinuria history must be: a documented history of proteinuria of > 1 g/day within 6 months prior to Screening, or urine protein/creatinine ratio (uPCR) > 0.75 by spot urine at Screening and mean proteinuria > 1 g/day at baseline.- Removed the upper cap on eGFR at Screening and baseline.- Deletion of the inclusion criterion specifying that the patient be: currently on physician-directed, stable treatment with RAS blockade and have a systolic BP of < 150 mm Hg and diastolic BP of < 100 mm Hg at rest.- Modification of the exclusion criterion for immunosuppressant use to narrow the disallowed window to 8 weeks from 24 weeks and to provide a caveat if the treatment is given for indications other than IgAN.- Modification of the exclusion criterion for corticosteroid use to narrow the disallowed window to within 8 weeks prior to Screening, previously within 12 weeks prior to Randomization.- Re-positioning of an inclusion criterion to exclusion criteria. The re-phrased criterion specifies the exclusion of patients who have: uncontrolled BP, a systolic BP of > 150 mm Hg and a diastolic BP of > 100 mm Hg at rest despite the combination of two or more anti-hypertensives including ACEIs, ARBs, or direct renin inhibitors.- Deletion of the exclusion criterion denying the participation of patients with a BMI \geq 35 kg/m².- Modified the retreatment following initial treatment. Instead of retreatment for 12 weeks, those with 24-hour UPE > 1 g/day after initial treatment will receive 6 weeks of extended treatment.- Changed the primary endpoint from 24 weeks to 36 weeks.- Revised the organization of the Secondary Endpoints from one list into Key Secondary Endpoints, Other Secondary Endpoints, and Safety and Other Endpoints.- Addition of new secondary endpoint.
19 February 2019	<p>Amendment#1 Continued...</p> <ul style="list-style-type: none">- Addition of new secondary endpoint: Time-averaged change from baseline in the log-transformed 24-hour UPE between 36 weeks and 48 weeks.- Addition of new secondary endpoint: Time-averaged change from baseline in the log-transformed 24-hour UPE between 36 weeks and 72 weeks.- Addition of new secondary endpoint: Time-averaged 24-hour UPE from 36 weeks to 48 weeks to a level at least 50% reduced from the baseline 24-hour UPE (patients with \geq 2 g/day UPE at baseline only).- Addition of new secondary endpoint: Time-averaged 24-hour UPE from 36 weeks to 72 weeks to a level at least 50% reduced from the baseline 24-hour UPE (patients with \geq 2 g/day UPE at baseline only).- Addition of new Safety and Other Endpoint: Change from baseline in log-transformed 24-hour uPCR over time.- Removed a secondary endpoint: Achievement of a partial response defined as a reduction between \geq 15% and < 30% from baseline in 24-hour UPE at 24 weeks.

19 February 2019	<p>Amendment #1:</p> <ul style="list-style-type: none"> - Increase in the number of study sites from 100 to 140 and addition of region (Asia). - Changed the primary objective from 24 weeks to 36 weeks from baseline. - Addition of new secondary objective: Durability of proteinuria response from 36 weeks. - Revised the secondary objective to assess proteinuria at 36 weeks (instead of 24 weeks) in the subset of patients with high baseline proteinuria. - Deleted secondary objectives: Per protocol defined responder at 24-weeks and per protocol defined partial responder at 24 weeks. - Moved secondary objective to other endpoints: Time-averaged change in urine protein/creatinine ratio (uPCR). - Moved secondary objective to other endpoints: Proportion of patients who achieve partial proteinuria remission (24-hour UPE < 0.6 g/day). - Moved secondary objective to other endpoints: Proportion of patients who achieve complete proteinuria remission (24-hour UPE < 0.3 g/day). - Moved secondary objective to other endpoints: Proportion of patients who received rescue therapy for IgAN at any time during the study. - Revision of the number of patients of special interest to be enrolled (those with a baseline 24-hour UPE \geq 2 g/day) from 50 to 78. - Run-In Period: Changed the length of the Run-In period to 4 weeks for those who have been on RAS blockade for 8 or more weeks, and to a 12-week Run-In for all other patients. - Response Evaluation Period: Changed the length of the Response Evaluation Period from Week 13 – Week 24 to Week 13 – Week 36. - Removed the description categories of responders, partial responders, and non-responders. - Deletion of Response Evaluation visits at Week 18 and 24. - Length of the Follow-Up Period was changed from 25 weeks – 144 weeks, to 37 weeks – 144 weeks. - Changed retreatment criteria at Week 24. - Modification of criteria for timing of rescue therapy. Also added the criteria that the patient has 100% increase in 24-hr UPE from baseline and patient has a 30% decrease in eGFR from baseline.
11 May 2020	<p>Amendment#2 Continued...</p> <ul style="list-style-type: none"> - Addition of text to the section entitled, Electrocardiogram, to note that at visits conducted virtually, this procedure will not be completed. - Addition of text to the section entitled, Laboratory Assessments, to note that at visits conducted virtually, it may be allowable for CMP, CBC+diff, UA, uACR, and uPCR to be performed by a local commercial laboratory in cases where the patient is unable to travel to the study site or the study site is unable to receive or process the samples for delivery to the central laboratory. - Addition of text to the section entitled, 24-hour Urine Collection. - Addition of language to section entitled, Serum and Urine Biomarkers and Antidrug Antibodies, to note that during the COVID-19 pandemic, it may be allowable for a commercial lab to prepare and ship protocol-specified biomarker samples, and if applicable, optional research biomarker samples, to the central laboratory. - Addition of language to section entitled, Run-In Visit 1 (RI1), that notes that this visit may be performed virtually (over the phone or video conference) or at the patient's home during the COVID-19 pandemic. - Addition of language to section entitled, Run-In Visit 2 (RI2), that notes that this visit may be performed at home during the COVID-19 pandemic regardless of whether the visit is an ongoing Run-In Visit or whether it is the final Run-In Visit. - Addition of language to section entitled, Run-In Visit 3 (RI3), that notes that this visit may be performed virtually (over the phone or video conference) or at the patient's home during the COVID-19 pandemic. - Addition of language to section entitled, Run-In Visit 4 (RI4), that notes that this visit may be performed at the patient's home during the COVID-19 pandemic. - Addition of language to section entitled, Treatment Visit 1 (T1/Week1) to note that randomization will not be repeated for patients who resume or reinitiate study treatment at T1.

11 May 2020	<p>Amendment#2 Continued...</p> <ul style="list-style-type: none"> - Addition of text to section entitled, Extended Treatment Following Week 12, to describe changes in Extended Treatment Period study visits and procedures during the COVID-19 pandemic. - Addition of text to describe changes in Response Evaluation study conduct during the COVID-19 pandemic. - Addition of language to the section entitled, Response Evaluation Telephone Calls (Weeks 16, 20, 24, 30 and 34) +/- 7 days, to note that the 24-hour urine collection specimen may be delivered to the study site or central lab by the specialty courier service selected by the sponsor, provided the patient has granted consent. - Addition of language to the section entitled, Response Evaluation Visit (Week 36) +/- 7 days Primary Endpoint, to describe changes in Response Evaluation study visits and procedures during the COVID-19 pandemic. - Addition of text to describe changes in Follow-Up Period study visits and procedures during the COVID-19 pandemic. - Addition of text to section entitled, Follow-Up Visits 1 and 3 (FU1 and FU3) (Week 48 and Week 96) +/- 14 days, to describe changes in study visits and procedures during the COVID-19 pandemic. - Addition of text to section entitled, Follow-Up Visits 2 and 4 (FU2 and FU4) (Week 72 and Week 120) +/- 14 days, to describe changes in study visits and procedures during the COVID-19 pandemic. - Addition of text to section entitled, Follow-Up Visit 5 (FU5/EOS) Week 144 +/- 14 days, to note that during the COVID-19 pandemic, FU5/EOS should be conducted at the study site in order to ensure completion of all required end of study assessments. - Addition of text to describe changes in 6-Week Relapse Retreatment Period study visits and procedures during the COVID-19 pandemic. - Addition of text to describe changes in 12-Week Relapse Retreatment Period study visits and procedures during the COVID-19 pandemic. - Addition of text to describe changes in Open-Label (OL) Extended Treatment Period study conduct during COVID-19.
11 May 2020	<p>Amendment#2 Continued...</p> <ul style="list-style-type: none"> - Addition of text to describe changes in Open-Label (OL) Relapse Retreatment Period study conduct during the COVID-19 pandemic. - Addition of text to section entitled, Timing of Study Procedures, to note that study procedures may be missed or delayed in which case the resulting protocol deviations must be clearly documented in source documents and the eCRF as related to the COVID-19 pandemic. - Addition of text to section entitled, Visit Windows, to note that study visits may be missed, canceled or delayed in which case the resulting protocol deviations must be clearly documented in source documents and the eCRF as related to the COVID-19 pandemic. - Addition of text to section entitled, Timing Between Assessments, to note that the timing of study procedures maybe impacted in which case the resulting protocol deviations must be clearly documented in source documents and the eCRF as related to the COVID-19 pandemic. - Addition of text to section entitled, Concomitant Therapy, to note that during delays in study visits as a result of the COVID-19 pandemic, investigators should make every effort to ensure patient adherence to the concomitant therapy requirements outlined in the protocol. - Addition of text to section entitled, Treatment Compliance, to note that study treatment visits may be missed or delayed in which case the resulting protocol deviations must be clearly documented in source documents and the eCRF as related to the COVID-19 pandemic. - Addition of text to section entitled, Adverse Event Reporting, to note that any COVID-19 related adverse events will be clearly documented as such in the source documents and the eCRF. - Addition of text to section entitled, General Considerations, to note that study week is defined from study Day 1 and will be determined by analysis visit windows which are defined approximately equally over adjacent scheduled visits.
11 May 2020	<p>Amendment#2 Continued...</p> <ul style="list-style-type: none"> - Addition of text to section entitled, Analysis of Primary Efficacy Endpoint, to note that the four timepoints will be determined from study Day 1 using analysis visit windows with equal width over adjacent visits. - Addition of text to the section entitled, Monitoring, to describe how study monitoring activities may be adjusted during the COVID-19 pandemic. - Addition of text to section entitled, Informed Consent Process, to note that during the COVID-19 pandemic, it may not be possible to obtain patient consent in person.

11 May 2020	<p>Amendment #2:</p> <ul style="list-style-type: none"> - Addition of text to highlight the changes made to protect patient safety during the COVID-19 pandemic. - Addition of text to describe changes in Screening Period activities during the COVID-19 pandemic. - Addition of text to describe changes in Run-In Period study visits and procedures during the COVID-19 pandemic. - Addition of text to describe changes in Initial Treatment Period study visits and procedures during the COVID-19 pandemic. - Addition of text to describe changes in Response Evaluation Period study conduct during the COVID-19 pandemic. - Addition of text to describe changes in Follow-Up study visits and procedures during the COVID-19 pandemic. - Addition of text to clarify that due to COVID-19 restrictions, patients who receive rescue therapy due to a treatment interruption of more than 2 consecutive study treatment visits may reinstate study treatment after completing a wash-out period of 8 weeks. - Addition of text to describe changes in Open-Label (OL) Treatment Period study visits and procedures during the COVID-19 pandemic. - Addition of footnote to exclusion criterion 15, previously received OMS721, stating that this criterion does not apply to patients who resume or reinstate study treatment after a COVID-19 related interruption. - Addition of text to section entitled, Informed Consent, to note that during the COVID-19 pandemic, it may not be possible to obtain patient consent in person. - Addition of text to the section entitled, Physical Examination, to note that at visits conducted virtually, the physical exam will not be completed. - Addition of text to the section entitled, Blood Pressure Optimization, to note that this procedure will be performed at virtual study visits. - Addition of text to the section entitled, Vital Signs, to note that during virtual study visits conducted during the COVID-19 pandemic, patients may obtain their blood pressure, pulse and oral body temperature using calibrated equipment provided to them.
04 November 2022	<p>Amendment #4: The following drug treatments are added to the exclusion criteria: 20. Treatment with sodium glucose co-transporter 2 inhibitors (SGLT2i) during Screening and Run-In Periods. However, a stable dose regimen established at least 8 weeks prior to Screening is acceptable. 21. Treatment with TARPEYO (budesonide) or other approved treatments for IgAN within 6 months prior to Screening. Treatment with TARPEYO is not allowed during Screening and Run-In Periods. -Treatment initiation during the study with SGLT2i or other drugs for the treatment of IgAN will result in early discontinuation of study drug treatment. - The following drug treatments are added to Concomitant Therapy: Treatment with sodium glucose co-transporter 2 inhibitors (SGLT2i) are prohibited from Screening onward. However, a stable dose regimen established at least 8 weeks prior to Screening is acceptable. Treatment with TARPEYO (budesonide) or other approved treatments for IgAN are prohibited within 6 months prior to Screening and throughout the study. Treatment with Kerendia (finerenone) is prohibited within 6 months prior to Screening and throughout the study.</p>
07 April 2023	<p>Amendment #5: - The number of study sites increased from 140 to 200. - The duration of the study decreased from 160 weeks to 112 weeks. -Primary objective to include patients with high baseline proteinuria. -Two key secondary objectives are added to evaluate renal function up to 96 weeks from baseline in patient with high baseline proteinuria and in all the patients population. - The key secondary objective to durability of proteinuria response from 36 weeks is clarified to define the population in which this objective will be evaluated (patients with high baseline proteinuria and in all the patients population) - The primary efficacy analysis is expected to include the upset of patients with 24 UPE. - A pre-blinded sample size re estimation as defined in the statistical analysis plan.- A conditional power based SSRE for the key second endpoint of EGFR is added. - Exclusion criteria #14 relative to treatment with sodium glucose cotransporter to inhibitor is changed.- Two Addition exclusion criteria are added to exclude. - Treatment with Chinese traditional medicine with immunosuppressive function is added and excluded medication. - Patient receiving sparsentan (Filspari) for a minimum of 12 weeks prior to screening will remain on this drug. - Endpoints are amended to align with the changes to objectives. - The sample size determination is further clarified. - Statistical methodology is added for multiple comparison and multiplicity. - Statistical methodology is added for analysis of primary and key secondary efficacy endpoints. - Analysis Population of for the FAS is clarified- an additional criteria for treatment discontinuation for patients who initiate treatment with SGLT2i or other drugs to treat IgAn</p>
09 May 2023	<p>Amendment #6: The Schedule of Events table for the open label extended treatment sub-group option has been added.</p>

19 June 2023	Amendment #7: -Text modification to exclusion criterion No. 20 (Section 8.2): • Treatment with or change in dosing of sodium glucose co-transporter 2 inhibitors (SGLT2i) during Screening and Run-In Periods. However, a stable dose regimen established at least 8 weeks prior to screening is acceptable. -Text modifications to Early Discontinuation of Study Drug Section 8.3.1): • The Investigator, Sponsor, or patient's primary care provider decides to discontinue treatment for medical reasons other than nonresponse to study treatment, or due to the patient's significant noncompliance with the protocol.
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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.

The study was terminated after the interim analysis due to the primary efficacy endpoint not being met, hence the data were not analyzed for secondary end points.

Notes: