



Clinical trial results:

REMODEL - Renal mode of action of semaglutide in patients with type 2 diabetes and chronic kidney disease

Summary

EudraCT number	2020-000828-19
Trial protocol	PL FR IT ES DK
Global end of trial date	21 November 2024

Results information

Result version number	v1 (current)
This version publication date	06 December 2025
First version publication date	06 December 2025

Trial information

Trial identification

Sponsor protocol code	NN9535-4662
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04865770
WHO universal trial number (UTN)	U1111-1248-7912

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Alle, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.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	13 June 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of once-weekly (OW) semaglutide administered subcutaneously (under the skin, s.c.) versus placebo on renal inflammation and haemodynamics, as measured by magnetic resonance imaging (MRI) in patients with type 2 diabetes (T2D) and chronic kidney disease (CKD).

Protection of trial subjects:

This study was conducted in accordance with the International Council for Harmonization (ICH) Good Clinical Practice (GCP), the Declaration of Helsinki, and US Food and Drug Administration (FDA) 21 US Code of Federal Regulations (CFR) 312.120. Essential documents will be maintained and archived in accordance with ICH GCP.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	28 April 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	United States: 36
Country: Number of subjects enrolled	South Africa: 7
Worldwide total number of subjects	106
EEA total number of subjects	55

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	46
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 31 sites in 8 countries.

Pre-assignment

Screening details:

Subjects were randomized in a 2:1 ratio to receive semaglutide or placebo, respectively. Both added to standard-of-care treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Semaglutide 1.0 mg
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Arm description:

Subjects received once-weekly (OW) subcutaneous (s. c.) injection of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Once-weekly subcutaneous injection of semaglutide was administered for 52 weeks.

Arm title	Placebo
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Arm description:

Subjects received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.

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

Dosage and administration details:

Once-weekly subcutaneous injection of placebo matched for semaglutide was administered for 52 weeks.

Number of subjects in period 1	Semaglutide 1.0 mg	Placebo
Started	71	35
Full analysis set	71	35
Safety analysis set	71	35
Completed	58	34
Not completed	13	1
Adverse event, serious fatal	1	1
Consent withdrawn by subject	3	-
Physician decision	9	-

Baseline characteristics

Reporting groups

Reporting group title	Semaglutide 1.0 mg
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Reporting group description:

Subjects received once-weekly (OW) subcutaneous (s. c.) injection of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.

Reporting group title	Placebo
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Reporting group description:

Subjects received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.

Reporting group values	Semaglutide 1.0 mg	Placebo	Total
Number of subjects	71	35	106
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	18	46
From 65-84 years	43	17	60
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	65.4	65.1	
standard deviation	± 9.2	± 11.3	-
Gender Categorical Units: Subjects			
Female	16	9	25
Male	55	26	81

End points

End points reporting groups

Reporting group title	Semaglutide 1.0 mg
Reporting group description: Subjects received once-weekly (OW) subcutaneous (s. c.) injection of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.	
Reporting group title	Placebo
Reporting group description: Subjects received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.	
Subject analysis set title	Semaglutide 1.0 mg/Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received OW treatment with 0.25 mg semaglutide or placebo from week 0 to week 4 followed by 0.5 mg semaglutide or placebo from week 4 to week 8 followed by 1 mg semaglutide or placebo from week 8 to week 52 depending on the arm they were randomised to. This arm has combined data from Semaglutide arm and Placebo arm.	

Primary: Change in kidney oxygenation (cortex), blood oxygenation-level dependent magnetic resonance imaging (BOLD MRI) (R2*)

End point title	Change in kidney oxygenation (cortex), blood oxygenation-level dependent magnetic resonance imaging (BOLD MRI) (R2*)
End point description: Change in kidney oxygenation in cortex assessed by BOLD (blood oxygenation level dependent) MRI from baseline (week 0) to end of treatment (week 52) is presented. R2* is a measure used in BOLD MRI to indicate the level of tissue oxygenation. A higher R2* value means lower tissue oxygenation while a lower R2* value means higher tissue oxygenation. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed = FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Primary
End point timeframe: From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of kidney oxygenation				
geometric mean (geometric coefficient of variation)				
Bilateral cortex (n = 58, 33)	0.98 (± 5.35)	1.00 (± 7.39)		
Right cortex (n = 58, 33)	0.98 (± 5.65)	0.99 (± 7.26)		
Left cortex (n = 58, 31)	0.98 (± 7.51)	1.01 (± 9.12)		

Statistical analyses

Statistical analysis title	Bilateral cortex
Statistical analysis description:	
The responses are analysed using an Analysis of covariance (ANCOVA) with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate, on log scale.	
Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1333
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.01

Statistical analysis title	Left cortex
Statistical analysis description:	
The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate, on log scale.	
Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0907
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1

Statistical analysis title	Right cortex
Statistical analysis description:	
The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate, on log scale.	
Comparison groups	Semaglutide 1.0 mg v Placebo

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2487
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.01

Primary: Change in kidney oxygenation (medulla), BOLD MRI (R2*)

End point title	Change in kidney oxygenation (medulla), BOLD MRI (R2*)
End point description:	
Change in kidney oxygenation in medulla assessed by BOLD MRI from baseline (week 0) to end of treatment (week 52) is presented. R2* is a measure used in BOLD MRI to indicate the level of tissue oxygenation. A higher R2* value means lower tissue oxygenation while a lower R2* value means higher tissue oxygenation. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Primary
End point timeframe:	
From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of kidney oxygenation (medulla)				
geometric mean (geometric coefficient of variation)				
Bilateral medulla (n = 57, 33)	0.99 (± 8.97)	1.01 (± 11.37)		
Right medulla (n= 57, 33)	0.98 (± 10.09)	1.02 (± 10.83)		
Left medulla (n= 58, 31)	0.99 (± 10.25)	1.02 (± 13.02)		

Statistical analyses

Statistical analysis title	Bilateral medulla
Statistical analysis description:	
The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.	
Comparison groups	Semaglutide 1.0 mg v Placebo

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5619
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.03

Statistical analysis title	Left medulla
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Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7924
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.04

Statistical analysis title	Right medulla
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Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2774
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.02

Primary: Change in global kidney perfusion (MRI)

End point title	Change in global kidney perfusion (MRI)
End point description:	
Change in global kidney perfusion assessed by phase contrast MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Primary
End point timeframe:	
From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of global kidney perfusion				
geometric mean (geometric coefficient of variation)				
Bilateral kidney (n = 49, 30)	1.03 (± 26.43)	0.99 (± 24.39)		
Right kidney (n = 50, 30)	1.04 (± 27.84)	0.98 (± 28.85)		
Left kidney (n = 50, 29)	1.02 (± 29.25)	1.01 (± 26.83)		

Statistical analyses

Statistical analysis title	Bilateral kidney
Statistical analysis description:	
The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.	
Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0958
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.24

Statistical analysis title	Right kidney
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Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0145
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.33

Statistical analysis title	Left kidney
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Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3311
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.21

Primary: Change in kidney inflammation (cortex), longitudinal relaxation time (T1) mapping (MRI)

End point title	Change in kidney inflammation (cortex), longitudinal relaxation
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End point description:

Change in kidney inflammation in cortex assessed by T1 mapping MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.

End point type

Primary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of kidney inflammation				
geometric mean (geometric coefficient of variation)				
Bilateral cortex (n = 56, 32)	1.01 (± 3.78)	1.01 (± 5.43)		
Right cortex (n = 56, 32)	1.01 (± 3.88)	1.01 (± 5.57)		
Left cortex (n = 56, 31)	1.01 (± 3.93)	1.01 (± 5.71)		

Statistical analyses

Statistical analysis title

Bilateral cortex

Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8651
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.02

Statistical analysis title

Left cortex

Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
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Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7195
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.02

Statistical analysis title	Right cortex
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Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.724
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.02

Primary: Change in kidney inflammation (medulla), T1 mapping (MRI)

End point title	Change in kidney inflammation (medulla), T1 mapping (MRI)
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End point description:

Change in kidney inflammation in medulla assessed by T1 mapping MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.

End point type	Primary
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End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of kidney inflammation (medulla)				
geometric mean (geometric coefficient of variation)				
Bilateral medulla (n = 56, 32)	1.00 (± 3.56)	1.00 (± 5.13)		
Right medulla (n = 56, 32)	1.00 (± 3.90)	1.01 (± 4.85)		
Left medulla (n = 56, 31)	1.00 (± 3.69)	1.00 (± 5.91)		

Statistical analyses

Statistical analysis title	Bilateral medulla
Statistical analysis description:	
The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.	
Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9335
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.02

Statistical analysis title	Left medulla
Statistical analysis description:	
The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.	
Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9017
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.02

Statistical analysis title	Right medulla
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Statistical analysis description:

The responses are analysed using an ANCOVA with actual treatment, region and the stratification factors as categorical effects and the baseline value as a covariate.

Comparison groups	Semaglutide 1.0 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6517
Method	ANCOVA
Parameter estimate	Treatment ratio
Point estimate	1

Confidence interval

level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.01

Secondary: Change in gene expression assessed by single nucleus ribonucleic acid (RNA) sequencing (kidney biopsy)

End point title	Change in gene expression assessed by single nucleus ribonucleic acid (RNA) sequencing (kidney biopsy)
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End point description:

Change in gene expression assessed by single nucleus RNA sequencing (kidney biopsy) from baseline (week 0) to end of treatment (week 52) is presented. Selected genes with a fold change >0.5 or <0.5 and a false discovery rate (FDR) <0.1 are presented to help identify biologically significant genes that are reliably differentially expressed in patients with conditions like Type 2 diabetes and chronic kidney disease. Data was annotated into different cell types. This was estimated with linear mixed model including subject as a random effect. These are all cell types that have differentially expressed genes that comply with threshold. This threshold is based on published in cross-sectional observational studies associated with disease impact around genes. FAS included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Overall 'Number subjects analyzed' = number of subjects with available data for particular timepoint, for the respective arms.

End point type	Secondary
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End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide 1.0 mg/Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: Log2 fold change				
number (not applicable)				
CNT-2, RSPO3	3.468216523			
CNT-Immune, SLC8A1-AS1	2.8531071			
EC-GC-1, KCNK6	-1.952545192			
EC-GC-1, EMC10	-2.485824696			
EC-GC-1, ENSG00000286145	1.831300888			
EC-GC-1, LMF1	-1.528463786			
EC-GC-1, ANKUB1	1.783402404			
EC-GC-1, AHNAK	-1.368952211			
EC-GC-1, ENSG00000286150	1.318309657			
EC-GC-1, NSUN6	-1.464540152			
EC-GC-1, TFCP2L1	-2.24516792			
EC-GC-1, ENSG00000274422	-1.860725608			
EC-GC-1, DPYD-AS1	1.996950045			
EC-GC-1, ENSG00000248138	2.110414741			
EC-GC-1, ACSM2B	-1.785467699			
EC-GC-1, CCNH	1.033873239			
EC-GC-1, QTRT1	-2.415240141			
EC-GC-1, CROCCP3	-1.254541813			
EC-GC-1, ENSG00000251034	1.750285729			
EC-GC-1, LSAMP	-2.439268964			
EC-GC-1, LHX1-DT	-4.256689925			
EC-GC-1, ESRRG	-1.527414037			
EC-GC-1, CNTNAP2	-2.377391827			
EC-GC-1, ENSG00000284966	1.665764749			
EC-GC-1, BICC1	-1.445239386			
EC-GC-1, GNA14-AS1	1.192645521			
EC-GC-1, GUSBP11	-1.318511642			
EC-GC-1, ENSG00000233783	1.668536087			
EC-GC-1, SEMA6A-AS1	1.183886707			
EC-GC-1, RBMS3-AS2	1.572052032			
EC-GC-1, ENSG00000286147	-4.468841041			
EC-GC-1, LINC00342	-1.151143461			
EC-GC-1, IRF3	-1.566408786			
EC-GC-1, ENSG00000249207	1.35685803			
EC-GC-1, CRADD-AS1	1.972404772			
EC-GC-1, TOX3	-2.206055055			
EC-GC-1, ENSG00000286458	1.271036656			
EC-GC-1, SLC12A3	-2.531722898			
EC-GC-1, TALAM1	1.235573321			
EC-GC-1, PCDH17	1.107442597			
EC-GC-1, ATP13A3	1.078246118			
EC-GC-1, ENSG00000231772	-2.382264501			
EC-GC-1, FBXL19	-2.166973377			
EC-GC-1, ENSG00000254420	1.74612131			
EC-GC-1, SPC25	1.329461228			
EC-GC-1, SMAD4	1.13655744			

EC-GC-1, UFM1	1.20264148			
EC-GC-1, ENSG00000259564	2.071724947			
EC-GC-1, SHOC1	1.634369451			
EC-GC-1, MEF2C-AS2	1.753288691			
EC-GC-1, ENSG00000285801	1.440844025			
EC-GC-1, FAM228B	-1.22996414			
EC-GC-1, GLS	0.868999317			
EC-GC-1, GDPD4	-6.564026305			
EC-GC-1, INSYN2A	1.759769032			
EC-GC-1, TNFRSF14	-1.254004029			
EC-GC-1, PRX	-1.199880651			
EC-GC-1, PNN	-1.024604708			
EC-GC-1, KCNQ1OT1	-0.794847103			
EC-GC-1, ACAP3	-1.44397269			
EC-GC-1, BASP1-AS1	-4.83539932			
EC-GC-1, RBFOX1	-1.706411849			
EC-GC-1, CCDC90B-AS1	-1.678217382			
EC-GC-1, ENSG00000240499	1.514399208			
EC-GC-1, LINC03076	1.545248095			
EC-GC-1, LINC01409	-1.022992954			
EC-GC-1, CCT4	1.455396063			
EC-GC-1, CDC73	0.802691458			
EC-GC-1, NUMA1	-0.931923316			
EC-GC-1, FLT4	-0.935590968			
EC-GC-1, PDLIM5	0.764926487			
EC-GC-1, SPCS3	1.02068757			
EC-GC-1, ENSG00000250646	1.917331079			
EC-GC-1, ENSG00000258168	1.083991656			
EC-GC-1, ST8SIA4	0.901071433			
EC-GC-1, BCL2L1-AS1	1.262413164			
EC-GC-1, NRSN2-AS1	-1.275348201			
EC-GC-1, STARD13-AS	1.148054491			
EC-GC-1, CFLAR-AS1	1.168941896			
EC-GC-1, PRKAR1A	1.257792414			
EC-GC-1, ENSG00000226239	1.126077043			
EC-GC-1, CTNNA3	-1.819759686			
EC-GC-1, KCNK5	-2.491597199			
EC-GC-1, ESR2	1.071576206			
EC-GC-1, SLC25A46	1.062235788			
EC-GC-1, REV3L	0.792446528			
EC-GC-1, ZC2HC1C	2.027909336			
EC-GC-1, ENSG00000279686	-1.453758633			
EC-GC-1, ACER1	-5.256214457			
EC-GC-1, MALRD1	-2.36001857			
EC-GC-1, RRBP1	-0.837125744			
EC-GC-1, ZNF451-AS1	1.853753635			
EC-GC-1, SHANK2	-1.481833304			
EC-GC-1, ENSG00000248388	2.196067138			
EC-GC-1, KPNA5	0.936135624			
EC-GC-1, APPAT	-1.750949862			
EC-GC-1, PCNT	-0.932423432			
EC-GC-1, ENSG00000233848	2.752498803			

EC-GC-1, MORF4L2	1.28059543			
EC-GC-1, ENSG00000236283	-1.572597604			
EC-GC-1, SNRNP70	-0.883484114			
EC-GC-1, EXD3	-0.805539835			
EC-GC-1, CNTNAP5	-2.392758482			
EC-GC-1, CASR	-2.323412555			
EC-GC-1, ENSG00000285692	1.124516569			
EC-GC-1, WDR81	-2.102548546			
EC-GC-1, ZNF160	-0.907890266			
EC-GC-1, CA12	-1.63720477			
EC-GC-1, MAPK8IP3	-0.998528168			
EC-GC-1, ABTB3	-2.945080572			
EC-GC-1, CHORDC1	1.047593755			
EC-GC-1, FREM1	-1.948982139			
EC-GC-1, FXVD6-AS1	2.22442108			
EC-GC-1, SPACA6	-1.045439073			
EC-GC-1, AGBL1	-2.851170905			
EC-GC-2, NES	-2.451444521			
EC-GC-2, ADARB2	-3.212266234			
EC-GC-2, SERPINB9	2.315559798			
EC-GC-2, ENSG00000274422	-2.329265154			
EC-GC-2, BTNL9	-2.01168798			
EC-GC-2, CPEB2	1.51543417			
EC-GC-2, TBX2	-2.604511077			
EC-GC-2, ENSG00000290560	2.378813977			
EC-GC-2, CFAP54	1.988387042			
EC-GC-2, ABI3BP	1.57362138			
EC-GC-2, SPACA6	-1.724379529			
EC-GC-2, ADAMTSL2	-2.009897896			
EC-GC-2, LZTS1	-2.659531511			
EC-GC-2, ENSG00000285744	1.889210245			
EC-GC-2, ENSG00000225689	-1.414674941			
EC-GC-2, LUZP2	-4.384000321			
EC-GC-2, NCKAP5	-1.592351284			
EC-GC-2, FAT1	-1.855192898			
NKC-NKT, AGBL4	-2.145446805			
NKC-NKT, TFEC	1.989578132			
NKC-NKT, ENSG00000254186	-2.913048038			
NKC-NKT, PDE10A	-2.170777761			
NKC-NKT, SHANK2	-2.431773845			
PEC, RGS6	-3.331377896			
PEC, AHNAK	-1.645129407			
PT-2, LRRC4C	-2.167101922			
PT-2, DSCAM	-3.104786855			
PT-2, RCN3	-1.636040003			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in glomerular basement membrane width (kidney biopsy)

End point title	Change in glomerular basement membrane width (kidney biopsy)
End point description: Change in glomerular basement membrane width assessed in kidney biopsy from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Overall 'Number subjects analyzed' = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Secondary
End point timeframe: From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: Nanometer (nm)				
arithmetic mean (standard deviation)	-72.67 (\pm 96.60)	-8.66 (\pm 206.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in apparent diffusion coefficient (ADC) (cortex) (MRI)

End point title	Change in apparent diffusion coefficient (ADC) (cortex) (MRI)
End point description: Change in apparent diffusion coefficient in cortex assessed by MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Secondary
End point timeframe: From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of ADC				
geometric mean (geometric coefficient of variation)				
Bilateral cortex (n = 51, 29)	1.00 (\pm 6.56)	0.94 (\pm 11.40)		
Left cortex (n= 52, 27)	1.01 (\pm 8.50)	0.96 (\pm 10.48)		

Right cortex (n = 52, 29)	0.98 (\pm 6.70)	0.93 (\pm 12.12)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Change in ADC (medulla) (MRI)

End point title	Change in ADC (medulla) (MRI)
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End point description:

Change in apparent diffusion coefficient in medulla assessed by MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.

End point type	Secondary
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End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of ADC				
geometric mean (geometric coefficient of variation)				
Bilateral medulla (n = 50, 29)	0.98 (\pm 8.90)	0.94 (\pm 13.51)		
Left medulla (n= 52, 27)	0.99 (\pm 9.51)	0.95 (\pm 13.41)		
Right medulla (n = 51, 29)	0.98 (\pm 10.00)	0.93 (\pm 13.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in mean renal artery resistive index (RARI) (MRI)

End point title	Change in mean renal artery resistive index (RARI) (MRI)
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End point description:

Change in renal arterial resistive index assessed by MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.

End point type	Secondary
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End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of RARI				
geometric mean (geometric coefficient of variation)				
Bilateral renalartery (n = 54, 32)	0.97 (± 7.00)	1.01 (± 6.13)		
Right renalartery (n = 56, 33)	0.98 (± 8.38)	1.01 (± 8.62)		
Left renalartery (n = 55, 30)	0.97 (± 7.44)	1.01 (± 6.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in mean arterial flow (MRI)

End point title	Change in mean arterial flow (MRI)
End point description:	
Change in mean arterial flow assessed by MRI from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analyzed= FAS. Number Analyzed(n) = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Secondary
End point timeframe:	
From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	35		
Units: Ratio of Mean arterial flow				
geometric mean (geometric coefficient of variation)				
Bilateral renalartery (n = 56, 32)	0.96 (± 24.96)	0.96 (± 25.06)		
Right renalartery (n = 56, 33)	0.97 (± 30.21)	0.95 (± 29.09)		
Left renalartery (n = 57, 30)	0.96 (± 25.06)	0.98 (± 27.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in natriuresis (urinary sodium excretion) (urinalysis)

End point title	Change in natriuresis (urinary sodium excretion) (urinalysis)
End point description:	
Change in natriuresis (urinary sodium excretion) (urinalysis) from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Overall 'Number subjects analyzed' = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Secondary
End point timeframe:	
From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	32		
Units: Millimoles per day (mmol/day)				
arithmetic mean (standard deviation)	-7.3 (± 71.3)	-26.9 (± 85.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in albumin excretion rate (urinalysis)

End point title	Change in albumin excretion rate (urinalysis)
End point description:	
Change in albumin excretion rate (urinalysis) from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Overall 'Number subjects analyzed' = number of subjects with available data for particular timepoint, for the respective arms.	
End point type	Secondary
End point timeframe:	
From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	33		
Units: Milligrams per day (mg/d)				
arithmetic mean (standard deviation)	-81.9 (± 708.8)	-233.2 (± 964.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in kidney function (creatinine clearance) (urinalysis)

End point title	Change in kidney function (creatinine clearance) (urinalysis)
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End point description:

Change in kidney function (creatinine clearance) (urinalysis) from baseline (week 0) to end of treatment (week 52) is presented. Full analysis set included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product. Overall 'Number subjects analyzed' = number of subjects with available data for particular timepoint, for the respective arms.

End point type	Secondary
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End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide 1.0 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	33		
Units: Milliliter per minute (ml/min)				
arithmetic mean (standard deviation)	3.8 (± 26.6)	-12.6 (± 34.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 57

Adverse event reporting additional description:

Safety analysis set. All presented TEAEs: AE with onset in all observed data points from 1st date of study product until permanent discontinuation of treatment. A subject died after discontinuing study by physician decision so counted in physician decision category in Subject Disposition in semaglutide arm.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received matching placebo to semaglutide s.c. once a week until week 52.

Reporting group title	Semaglutide 1.0 mg
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Reporting group description:

Subjects received escalated dose of semaglutide subcutaneously (s.c.) (0.25, 0.5, milligrams [mg]) once weekly for 8 weeks followed by a maintenance dose of semaglutide 1.0 mg s.c. once weekly until week 52.

Serious adverse events	Placebo	Semaglutide 1.0 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 35 (14.29%)	14 / 71 (19.72%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal cell carcinoma			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			

subjects affected / exposed	1 / 35 (2.86%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 35 (2.86%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Anger			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			

subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhagic stroke			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			

subjects affected / exposed	1 / 35 (2.86%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 35 (0.00%)	4 / 71 (5.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 35 (2.86%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Osteomyelitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	0 / 35 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Semaglutide 1.0 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 35 (31.43%)	15 / 71 (21.13%)	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	2 / 35 (5.71%)	4 / 71 (5.63%)	
occurrences (all)	2	4	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 35 (5.71%)	4 / 71 (5.63%)	
occurrences (all)	2	5	
Diarrhoea			
subjects affected / exposed	4 / 35 (11.43%)	4 / 71 (5.63%)	
occurrences (all)	5	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 35 (0.00%)	4 / 71 (5.63%)	
occurrences (all)	0	4	
Upper respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	1 / 71 (1.41%)	
occurrences (all)	2	1	
Nasopharyngitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 35 (0.00%)	4 / 71 (5.63%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2021	To align minimum requirements for the kidney biopsy sites, kidney biopsy procedure and sponsor oversight. In addition, one randomisation criteria was added to ensure stable dose of RAAS blocking agent between screening and randomisation.
24 May 2022	To update few inclusion criteria as it is expected to beneficially impact on recruitment without compromising the study integrity or subject safety. Minor editorial changes were made to increase consistency and clarity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported