



Clinical trial results: Lumasiran in hyperoxalaemic patients on haemodialysis Summary

EudraCT number	2022-002681-32
Trial protocol	DE
Global end of trial date	20 January 2025

Results information

Result version number	v1 (current)
This version publication date	20 February 2026
First version publication date	20 February 2026

Trial information

Trial identification

Sponsor protocol code	20018510
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT06225544
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Gerlineke Hawkins-van der Cingel, Campus Virchow-Klinikum Medizinische Klinik m.S. Nephrologie und Internistische Intensivmedizin, 49 304507530067, gerlineke.hawkins-van- der-cingel@charite.de
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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	16 December 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 January 2025
Global end of trial reached?	Yes
Global end of trial date	20 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess if this medication can successfully lower plasma oxalate levels in patients with End Stage Kidney Disease on haemodialysis.

Protection of trial subjects:

The study was conducted in accordance with the ICH E6 (R2) Guideline for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, German Medicinal Products Act (AMG)), and with the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy:

Cardiovascular death remains the leading cause of mortality for patients with ESKD, with minimal advances to ameliorate this in recent years. Whilst traditional risk factors such as hypercholesterolemia and atherosclerosis are important, this does not fully explain the significantly increased risk for patients with ESKD. In the general population, the main causes of cardiovascular death are stroke and myocardial infarction, however the dialysis population is more likely to die from sudden cardiac death or recurrent heart failure.

There is increasing scientific evidence that aside from traditional cardiovascular risk factors such as altered lipid metabolism; the dysregulated metabolism of certain amino acids play a role in inflammation and atherosclerosis. Reduced glycine-oxalate ratios have been demonstrated in both human and mice models with atherosclerosis. AGXT is a main driver of glycine biosynthesis and when deficient leads to rising glyoxylate which is subsequently converted to oxalate. In brief, this triggers pro-atherogenic pathways, increased inflammatory pathway signalling and superoxide accumulation.

From our own preliminary studies we know that pre-dialysis oxalate levels do recover between dialysis sessions, indicating that supra-normal oxalate levels persist for the majority of the time for our patients. As laboratory work continues to investigate the role of oxalate in atherosclerosis, there remains limited improvements in cardiovascular outcomes for haemodialysis patients over recent decades. If this preliminary study can show that a new oxalate lowering agent is well tolerated and efficacious in this population, it would pave the way for larger trials to establish if lowering excessive serum oxalate can successfully lower cardiovascular mortality and morbidity.

Evidence for comparator: -

Actual start date of recruitment	01 March 2024
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	Germany: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	15
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 2 site in Germany from March 1, 2024 to January 20, 2025.

Pre-assignment

Screening details:

36 patients were screened aged between ≥ 18 and ≤ 80 years old with ESKD and who are receiving chronic haemodialysis treatment, of whom 29 were randomised.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group

Arm description:

Lumasiran, an RNA interference (RNAi) therapeutic agent.

Lumasiran targets the HAO1 gene (hydroxyacid oxidase 1 gene) which encodes glycolate oxidase. By degrading the mRNA for glycolate oxidase, this reduces the hepatic production of oxalate and increases the concentration of its precursor glycolate which is more readily excreted. Thus, reducing both the urinary and plasma oxalate levels.

Lumasiran is conjugated to GalNAc which is a carbohydrate with a very high affinity for a highly expressed receptor in the liver, allowing for a targeted delivery system to the liver.

Arm type	Experimental
Investigational medicinal product name	Lumasiran
Investigational medicinal product code	EMA/H/C/005040
Other name	Lumasiran sodium
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Lumasiran was injected at the end of the dialysis session at a dose of 3mg/kg, monthly loading doses for 3 months followed by the first of the quarterly maintenance doses starting a month after the last loading dose.

Patients received at the end of the first haemodialysis session of the week (i.e., after the long interval, either on a Monday or Tuesday).

loading dose

Arm title	Placebo
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Arm description: -

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:

Placebo (0.9% Sodium Chloride) was injected at the end of the dialysis session. It was given given as three monthly loading doses followed by one further maintenance dose.

Number of subjects in period 1	Treatment group	Placebo
Started	16	13
Completed	13	13
Not completed	3	0
Adverse event, serious fatal	2	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Treatment group
Reporting group description:	
Lumasiran, an RNA interference (RNAi) therapeutic agent. Lumasiran targets the HAO1 gene (hydroxyacid oxidase 1 gene) which encodes glycolate oxidase. By degrading the mRNA for glycolate oxidase, this reduces the hepatic production of oxalate and increases the concentration of its precursor glycolate which is more readily excreted. Thus, reducing both the urinary and plasma oxalate levels. Lumasiran is conjugated to GalNAc which is a carbohydrate with a very high affinity for a highly expressed receptor in the liver, allowing for a targeted delivery system to the liver.	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Treatment group	Placebo	Total
Number of subjects	16	13	29
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	56.8	66.7	
standard deviation	± 14.6	± 12.7	-
Gender categorical			
Units: Subjects			
Female	6	5	11
Male	10	8	18
Diabetes mellitus Type 2			
Comorbidities			
Units: Subjects			
No	13	11	24
Yes	3	2	5
Ischaemic heart failure			
Comorbidities			
Units: Subjects			
No	10	8	18
Yes	6	5	11
Stroke			
Comorbidities			
Units: Subjects			

No	14	12	26
Yes	2	1	3
Peripheral vascular disease			
Comorbidities			
Units: Subjects			
No	11	10	21
Yes	5	3	8
Cardiac arrhythmia (no further specified)			
Comorbidities			
Units: Subjects			
No	13	9	22
Yes	3	4	7
Acute coronary syndrom			
Comorbidities			
Units: Subjects			
No	16	12	28
Yes	0	1	1
Structural heart disease			
Comorbidities			
Units: Subjects			
No	11	7	18
Yes	5	6	11
Renal history - Cause of ESKD			
*Other causes including: Obstructive disease/nephrectomy, IgA Nephropathy, FSGS, AA Amyloid, MCGN, Bartter syndrome, recurrent AKI & TIN			
Units: Subjects			
Diabetic nephropathy	2	2	4
Other causes including*	13	6	19
Polycystic kidney disease, autosomal dominant	0	2	2
Systemic lupus erythematosus	1	1	2
CKDu	0	2	2
Transplantation history			
Units: Subjects			
No	16	10	26
Yes	0	3	3
Current HD Access			
Units: Subjects			
Tunnelled haemodialysis catheter (THL)	5	2	7
Arteriovenous fistula (AVF)	8	9	17
Arteriovenous graft (AVG)	3	2	5
Beta blocker			
Regular Medications			
Units: Subjects			
No	4	3	7
Yes	12	10	22
ACE inhibitors / ARB			
Regular Medications			
Units: Subjects			
No	6	4	10

Yes	10	9	19
Anti-platelets			
Regular Medications			
Units: Subjects			
No	12	9	21
Yes	4	4	8
Anti-coagulation			
Units: Subjects			
No	10	10	20
Yes	6	3	9
Statins			
Units: Subjects			
No	11	8	19
Yes	5	5	10
24h urine volume			
Units: Subjects			
400 ml	1	0	1
500 ml	3	0	3
Anuric	12	13	25
BMI			
Units: kg/m ²			
arithmetic mean	26.1	24.6	-
standard deviation	± 5.8	± 4.1	-
Systolic blood pressure			
Units: mmHg			
arithmetic mean	134.8	133.8	-
standard deviation	± 24.6	± 18.2	-
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	74.4	66	-
standard deviation	± 17.8	± 15.6	-
Duration of dialysis			
Units: year			
arithmetic mean	20.8	18	-
standard deviation	± 2.7	± 5.4	-
Current average clearance			
Units: Kt/v			
arithmetic mean	1.4	1.5	-
standard deviation	± 0.4	± 0.2	-
Average IDW gains			
Units: kg			
arithmetic mean	2.2	2.7	-
standard deviation	± 0.7	± 0.8	-
Plasma Oxalate level			
Units: µmol/L			
arithmetic mean	40.7	33.7	-
standard deviation	± 19.5	± 6.4	-

End points

End points reporting groups

Reporting group title	Treatment group
Reporting group description: Lumasiran, an RNA interference (RNAi) therapeutic agent. Lumasiran targets the HAO1 gene (hydroxyacid oxidase 1 gene) which encodes glycolate oxidase. By degrading the mRNA for glycolate oxidase, this reduces the hepatic production of oxalate and increases the concentration of its precursor glycolate which is more readily excreted. Thus, reducing both the urinary and plasma oxalate levels. Lumasiran is conjugated to GalNAc which is a carbohydrate with a very high affinity for a highly expressed receptor in the liver, allowing for a targeted delivery system to the liver.	
Reporting group title	Placebo
Reporting group description: -	

Primary: change Plasma Oxalate Levels by group and time point

End point title	change Plasma Oxalate Levels by group and time point
End point description:	
End point type	Primary
End point timeframe: from baseline up to 6 months	

End point values	Treatment group	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14 ^[1]	13		
Units: µmol/L				
arithmetic mean (standard deviation)				
Month 1	4.9 (± 19)	1.5 (± 5.1)		
Month 2	10.6 (± 20.8)	4.7 (± 4.1)		
Month 3	1.4 (± 8.3)	4.1 (± 5.4)		
Month 4	1.4 (± 9.3)	5.3 (± 5.7)		
Month 5	5.1 (± 7.8)	1.6 (± 7.6)		
Month 6	2.7 (± 6.7)	-3 (± 14)		

Notes:

[1] - n= 14 Month 1-2 und

n= 13 Month 3-6, because one person less due to lack of compliance

Statistical analyses

Statistical analysis title	Percentage change of plasma oxalate level
Statistical analysis description: The primary analysis (FAS) .The treatment effect along with a 95% confidence interval was estimated from a linear mixed model with percentage change of plasma oxalate level as response, and with treatment, time and their interaction as fixed effects, and patient as random effect adjusted for baseline plasma oxalate level. All estimates will be accompanied with 95% confidence intervals. The imputation was done separately by group.	
Comparison groups	Treatment group v Placebo

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall trial

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	5.0
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Reporting groups

Reporting group title	Treatment group
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Treatment group	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 16 (25.00%)	4 / 13 (30.77%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic Urothelial carcinoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Fracture	Additional description: Fracture fibula		
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischemia	Additional description: Acute limb ischaemia due to occlusion of right sided limb of EVAR prosthesis		
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Bowel resection after bowel ischemia subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elective femoral-popliteal bypass subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders Myocardial infarction subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
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 Multi-organ failure subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders pneumonia, atypical subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Treatment group	Placebo	
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 16 (6.25%)	1 / 13 (7.69%)	
Skin and subcutaneous tissue disorders Pruritus	Additional description: Mild itching		
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Covid-19 infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 13 (7.69%) 1	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 April 2024	change of Chief Investigator

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 planned recruitment number was not achieved. The reasons were the burden of comorbidity, particularly psychiatric comorbidity and reluctance for an injection/health anxiety post the COVID-19 pandemic.

Notes: