Clinical trial results:
Hyperpolarized xenon lung MRI in long-term COVID19

Summary

EudraCT number	2021-006335-26
Trial protocol	DK
Global end of trial date	05 September 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	Xe-long-COVID

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus, Denmark, 8200
Public contact	MR Research Center, Aarhus University, cl@clin.au.dk
Scientific contact	MR Research Center, Aarhus University, cl@clin.au.dk

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	05 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 August 2024
Global end of trial reached?	Yes
Global end of trial date	05 September 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To study lung gas uptake in long COVID19

Protection of trial subjects:

All subject were thoroughly screened for MRI contraindications.
During IMP inhalation, peripheal saturation was continuously monitored, and subjects were instructed to resume breathing if the saturation dropped below 85% or more than 5%-points.

Background therapy: -

Evidence for comparator:

An age and gender matched control group was recruited to compare to the gas transfer of patients

Actual start date of recruitment	01 July 2023
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	Denmark: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	19
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were contacted through the long covid-19 clinic, at the department of infectious diseases, Aarhus University hospital. Healthy through public advertisement. If a subject was interested in participation, they were contacted by sponsors representative to elaborate on the study. If still interested, a date for inclusion was set as appropriate

Pre-assignment

Screening details:

Screening was based on the patient self reported health scales with medical research council score above 2.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Explorative physiological study

Arms

Are arms mutually exclusive?	Yes
Arm title	Patients

Arm description:

PAtients with Post COVID-19 Condition with MRC dyspnea above 2

Arm type	Experimental
Investigational medicinal product name	xenon
Investigational medicinal product code	PRD10485456
Other name	Xenon-129
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

For subjects of height 160 cm and above: 500 ml mixed with 500 ml nitrogen.
For subjects of height 150 cm till 160 cm: 450ml mixed with 350 ml nitrogen.

Arm title	Healthy Controls

Arm description:

Healthy age and gender matched controls

Arm type	Active comparator
Investigational medicinal product name	Xenon
Investigational medicinal product code	PRD10485456
Other name	Xenon-129
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

For subjects of height 160 cm and above: 500 ml mixed with 500 ml nitrogen.
For subjects of height 150 cm till 160 cm: 450ml mixed with 350 ml nitrogen.

Number of subjects in period 1	Patients	Healthy Controls
Started	14	8
Completed	14	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	22	22	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	19	19	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	16	16	
Male	6	6	

Subject analysis sets	
Subject analysis set title	Patients
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients	
Subject analysis set title	Healthy Controls
Subject analysis set type	Sub-group analysis
Subject analysis set description: Healthy Controls	

Reporting group values	Patients	Healthy Controls	
Number of subjects	14	8	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	7	

From 65-84 years	2	1	
85 years and over	0	0	

Gender categorical Units: Subjects			
Female	11	5	
Male	3	3	

End points

End points reporting groups

Reporting group title	Patients
Reporting group description: PAtients with Post COVID-19 Condition with MRC dyspnea above 2	
Reporting group title	Healthy Controls
Reporting group description: Healthy age and gender matched controls	
Subject analysis set title	Patients
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients	
Subject analysis set title	Healthy Controls
Subject analysis set type	Sub-group analysis
Subject analysis set description: Healthy Controls	

Primary: Lung gas uptake and structure assessed with hyperpolarized xenon MRI

End point title	Lung gas uptake and structure assessed with hyperpolarized xenon MRI
End point description:	
End point type	Primary
End point timeframe: at day of examination	

End point values	Patients	Healthy Controls	Patients	Healthy Controls
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	12	8	12	8
Units: percent				
number (not applicable)				
RBC:M	0.214617	0.243863	0.214617	0.243863
RBC:GAS	0.001653	0.001629	0.001653	0.001629
M:GAS	0.007030	0.006251	0.007030	0.006251

Statistical analyses

Statistical analysis title	RBC:M
Comparison groups	Healthy Controls v Patients

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.305
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Point estimate	0.0292
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0191
upper limit	0.107

Statistical analysis title	RBG:GAS
Comparison groups	Patients v Healthy Controls v Patients v Healthy Controls
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.97
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-0.0000087
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.000414
upper limit	0.000492

Statistical analysis title	M:GAS
Comparison groups	Patients v Healthy Controls v Patients v Healthy Controls
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.172
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-0.000779
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.00194
upper limit	0.000377

Secondary: Lung Mircrostrucure

End point title	Lung Mircrostrucure
End point description: The Apparent Diffusion Coefficient (ADC) and the mean diffusive length scale (LmD) are measures if lung alveolar size	
End point type	Secondary
End point timeframe: At time of examination	

End point values	Patients	Healthy Controls		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: micrometre(s)				
median (inter-quartile range (Q1-Q3))				
LmD	283.8 (272.4 to 295.1)	297.7 (294.4 to 318.2)		
ADC	0.035 (0.033 to 0.037)	0.039 (0.038 to 0.043)		

Statistical analyses

Statistical analysis title	ADC
Comparison groups	Patients v Healthy Controls
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.012
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.00486
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.00122
upper limit	0.0085

Statistical analysis title	LmD
Comparison groups	Patients v Healthy Controls
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.013
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	22.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.37
upper limit	39.6

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
On the date of examination	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	Patients
Reporting group description:	
PAtients with Post COVID-19 Condition with MRC dyspnea above 2	
Reporting group title	Healthy Controls
Reporting group description:	
Healthy age and gender matched controls	

Serious adverse events	Patients	Healthy Controls	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Patients	Healthy Controls	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 14 (57.14%)	4 / 8 (50.00%)	
Nervous system disorders			
Sensory disturbance			
subjects affected / exposed	2 / 14 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Dizziness			
subjects affected / exposed	4 / 14 (28.57%)	3 / 8 (37.50%)	
occurrences (all)	4	3	
Gastrointestinal disorders			
Epigastric discomfort			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Taste disorder	Additional description: taste of metal		
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Study was terminated early due to slow recruitment. This lead to a smaller than desired sample size.

Notes: