



## Clinical trial results: The Estimated 12-Hour Serum Lithium Level Pilot Study Summary

EudraCT number	2022-000034-42
Trial protocol	DK
Global end of trial date	27 June 2023

### Results information

Result version number	v1 (current)
This version publication date	15 October 2024
First version publication date	15 October 2024

### Trial information

#### Trial identification

Sponsor protocol code	2022-001
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Aarhus University Hospital Psychiatry
Sponsor organisation address	Palle Juul-Jensens, Aarhus, Denmark,
Public contact	Ole Köhler-Forsberg, Aarhus University Hospital - Psychiatry, Department of Affective Disorders, 0045 23420661, karkoe@rm.dk
Scientific contact	Ole Köhler-Forsberg, Aarhus University Hospital - Psychiatry, Department of Affective Disorders, 0045 23420661, karkoe@rm.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	03 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2023
Global end of trial reached?	Yes
Global end of trial date	27 June 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To investigate the distribution of serum lithium levels during the 24 hours after the most recent lithium dose.

Protection of trial subjects:

Trial participation involved 9 blood tests over a period of 24 hours, including late at night and early morning. For each participant, we evaluated whether it was necessary to wake patients early in the morning. If it was deemed unsafe for the participant, we skipped this blood test.

Background therapy:

Treatment-as-usual based on clinical indication

Evidence for comparator: -

Actual start date of recruitment	15 April 2022
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	Denmark: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	21
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients on a stable dose of lithium

### Pre-assignment

Screening details:

1. Age  $\geq 18$  years.
2. Treatment with lithium.
3. On a stable lithium dose, i.e., no dose change within the past 5 days.
4. Lithium prescribed as one daily dose administered in the evening.

### Period 1

Period 1 title	eLi12 validation trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	Lithium
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Arm description:

On a stable dose of lithium

Arm type	Experimental
Investigational medicinal product name	Lithium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Stable dose of lithium, no predefined dose. The individual dose was based on clinical indication.

<b>Number of subjects in period 1</b>	Lithium
Started	23
Completed	23

## Baseline characteristics

### Reporting groups

Reporting group title	eLi12 validation trial
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Reporting group description: -

Reporting group values	eLi12 validation trial	Total	
Number of subjects	23	23	
Age categorical			
Participants were aged between 21 and 72 years. Mean age 41.6 years.			
Units: Subjects			
Adults 18-72 years	23	23	
Gender categorical			
14 participants were females, 9 were males			
Units: Subjects			
Female	14	14	
Male	9	9	

### Subject analysis sets

Subject analysis set title	Analysis on all participants
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Subject analysis set type	Full analysis
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Subject analysis set description:

When including all blood tests (excluding those at 0 and 12 hours), the mean difference from the measured se-Li compared to the 12-hour se-Li level was 0.14 mEq/L, while the difference was 0.07 mEq/L for eLi12 ( $p < 0.0001$ ). The difference between the measured se-Li and the 12-hour level was larger at the more extreme time points, e.g., at 4, 19 or 20 hours, with eLi12 being notably closer to the 12-hour se-Li level even at these extreme time points. For example, after 20 hours, the measured mean se-Li was 0.21 (34%) lower than the 12-hour se-Li level, while the mean eLi12 was only 0.07 (12%) lower.

Among blood tests taken between 3 and 24 hours after the most recent lithium dose, 99 out of 102 (97%) eLi12 estimations were closer to the 12-hour se-Li compared to the measured se-Li concentrations. At no time point did eLi12 estimate an unexpectedly high 12-hour se-Li level.

Reporting group values	Analysis on all participants		
Number of subjects	23		
Age categorical			
Participants were aged between 21 and 72 years. Mean age 41.6 years.			
Units: Subjects			
Adults 18-72 years	23		
Gender categorical			
14 participants were females, 9 were males			
Units: Subjects			
Female	14		
Male	9		

## End points

### End points reporting groups

Reporting group title	Lithium
Reporting group description: On a stable dose of lithium	
Subject analysis set title	Analysis on all participants
Subject analysis set type	Full analysis
Subject analysis set description: When including all blood tests (excluding those at 0 and 12 hours), the mean difference from the measured se-Li compared to the 12-hour se-Li level was 0.14 mEq/L, while the difference was 0.07 mEq/L for eLi12 ( $p < 0.0001$ ). The difference between the measured se-Li and the 12-hour level was larger at the more extreme time points, e.g., at 4, 19 or 20 hours, with eLi12 being notably closer to the 12-hour se-Li level even at these extreme time points. For example, after 20 hours, the measured mean se-Li was 0.21 (34%) lower than the 12-hour se-Li level, while the mean eLi12 was only 0.07 (12%) lower. Among blood tests taken between 3 and 24 hours after the most recent lithium dose, 99 out of 102 (97%) eLi12 estimations were closer to the 12-hour se-Li compared to the measured se-Li concentrations. At no time point did eLi12 estimate an unexpectedly high 12-hour se-Li level.	

### Primary: eLi12

End point title	eLi12
End point description: The primary endpoint was whether eLi12 could estimate a 12-hour se-Li level within an acceptable range of the measured 12-hour se-Li level without giving falsely high or low se-Li values. All se-Li data from participants with a measured se-Li level at 12 hours and at least one other time point was included for analyses.	
End point type	Primary
End point timeframe: For each participant, we took blood tests during 24 hours after the lithium dose.	

End point values	Lithium	Analysis on all participants		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	23	23		
Units: mEq/L				
number (not applicable)	23	23		

### Statistical analyses

Statistical analysis title	Statistical analyses
Comparison groups	Lithium v Analysis on all participants
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.08
Variability estimate	Standard deviation
Dispersion value	0.01

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

During participation and the subsequent 3 days.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.0
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### Reporting groups

Reporting group title	Adverse events
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Reporting group description: -

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no non-serious adverse events

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported