



Clinical trial results:

Efficacy of ALXN1840 on human biliary copper excretion quantified with ⁶⁴CuCl₂ PET/MR-scan

Summary

EudraCT number	2021-000102-25
Trial protocol	DK
Global end of trial date	04 July 2022

Results information

Result version number	v1 (current)
This version publication date	03 January 2024
First version publication date	03 January 2024

Trial information

Trial identification

Sponsor protocol code	ALXN1840-WD-Cu-Excretion
-----------------------	--------------------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark,
Public contact	Public information about the trial., Aarhus University Hospital, thomsand@rm.dk
Scientific contact	Public information about the trial., Aarhus University Hospital, thomsand@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	20 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2022
Global end of trial reached?	Yes
Global end of trial date	04 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate whether ALXN1840 increases biliary copper excretion in Wilson's Disease patients.

Protection of trial subjects:

Blood samples before and after treatment, including liver, kidney and hematological parameters. Only inclusion of stable patients as evaluated by clinical physicians. Medical supervision during tracer injection and scans. Participants given contact information of medical personnel and instructed to note all adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2021
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: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	4
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participating patients were recruited from the outpatient clinic at the Department of Hepatology and Gastroenterology, Aarhus University Hospital after clinical assessment of disease stability. The diagnosis was confirmed in accordance with the Leipzig criteria.

Pre-assignment

Screening details:

Interested patients were evaluated for stability, length and choice of current Wilson treatment and after this receive the full study participant information and material. If still interested they would be contacted by telephone and finally be invited for a face-to-face meeting and inclusion into the study.

Period 1

Period 1 title	Pre-treatment
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Pre-treatment
Arm description: -	
Arm type	Baseline, pre-treatment
Investigational medicinal product name	ALXN1840
Investigational medicinal product code	
Other name	Bis-choline tetrathiomolybdate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg once daily, oral. Fast one hour before and after each dose.

Number of subjects in period 1	Pre-treatment
Started	5
Completed	4
Not completed	1
Consent withdrawn by subject	1

Period 2

Period 2 title	Post-treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Arm title	Post-treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	ALXN1840
Investigational medicinal product code	
Other name	Bis-choline tetrathiomolybdate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg once daily, oral. Fast one hour before and after each dose.

Number of subjects in period 2	Post-treatment
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Pre-treatment
-----------------------	---------------

Reporting group description: -

Reporting group values	Pre-treatment	Total	
Number of subjects	5	5	
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)	4	4	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	4	4	
Alanine aminotransferase			
Units: U/L			
median	39.50		
inter-quartile range (Q1-Q3)	25.50 to 59.00	-	
Bilirubine			
Units: umol/L			
median	9.50		
inter-quartile range (Q1-Q3)	7.00 to 16.50	-	
Creatinine			
Units: umol/L			
median	63.00		
inter-quartile range (Q1-Q3)	58.00 to 72.00	-	
P-copper			
Units: umol/L			
median	2.45		
inter-quartile range (Q1-Q3)	1.30 to 5.30	-	

End points

End points reporting groups

Reporting group title	Pre-treatment
Reporting group description: -	
Reporting group title	Post-treatment
Reporting group description: -	

Primary: Gallbladder

End point title	Gallbladder
End point description: Multiple scans during the study period both before and after treatment.	
End point type	Primary
End point timeframe: 1 - 68H after tracer injection.	

End point values	Pre-treatment	Post-treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1H	2.17 (1.08 to 2.97)	1.31 (0.85 to 1.88)		
2H	3.44 (2.22 to 4.00)	2.06 (1.25 to 2.23)		
6H	3.10 (3.02 to 3.22)	1.98 (1.21 to 2.48)		
20H	3.27 (2.58 to 4.33)	2.44 (1.63 to 4.11)		
48H	2.80 (2.58 to 3.38)	2.55 (2.49 to 3.10)		
54H	3.03 (2.56 to 4.06)	3.05 (2.44 to 3.70)		
68H	2.15 (1.18 to 3.76)	2.78 (1.77 to 3.37)		

Statistical analyses

Statistical analysis title	Statistical test
Statistical analysis description: Each of the four subjects acted as their own control. Pre vs post-treatment.	
Comparison groups	Pre-treatment v Post-treatment

Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05 ^[1]
Method	Sign test

Notes:

[1] - At time 1, 2, 20, 48, 54, 68 hours since tracer injection, $p > 0.05$ (Non-significant).

At time 6 hours since tracer injection, $p = 0.0209$ (Significant reduction in gallbladder SUV on TTM).

Secondary: Liver

End point title	Liver
-----------------	-------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

1 - 68H post tracer injection.

End point values	Pre-treatment	Post-treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1H	17.77 (16.67 to 21.19)	7.44 (5.96 to 8.97)		
2H	21.77 (19.54 to 24.23)	8.76 (7.95 to 10.77)		
6H	27.11 (24.30 to 32.08)	14.30 (13.32 to 16.83)		
20H	33.57 (29.80 to 38.42)	22.59 (19.38 to 26.09)		
48H	37.71 (34.66 to 40.70)	28.93 (26.63 to 29.53)		
54H	36.41 (32.16 to 41.52)	27.22 (24.65 to 29.06)		
68H	38.66 (34.67 to 43.54)	28.48 (25.41 to 31.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kidney

End point title	Kidney
-----------------	--------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

1 - 68H post tracer injection.

End point values	Pre-treatment	Post-treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1H	7.23 (6.61 to 9.27)	6.87 (6.28 to 9.27)		
2H	5.59 (5.17 to 8.89)	6.78 (6.52 to 9.25)		
6H	4.81 (3.93 to 7.06)	9.05 (7.92 to 11.30)		
20H	2.79 (2.36 to 3.85)	10.59 (9.24 to 11.34)		
48H	1.63 (1.38 to 2.10)	12.72 (11.25 to 14.02)		
54H	1.73 (1.52 to 1.95)	12.77 (10.39 to 14.88)		
68H	1.45 (1.13 to 1.96)	11.77 (11.19 to 12.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pancreas

End point title	Pancreas
End point description:	
End point type	Secondary
End point timeframe:	
1 - 68H post tracer injection.	

End point values	Pre-treatment	Post-treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1H	7.65 (5.67 to 14.02)	4.96 (4.25 to 6.94)		
2H	7.60 (5.85 to 12.49)	4.36 (3.65 to 5.36)		
6H	4.37 (2.98 to 9.50)	4.69 (3.24 to 5.82)		
20H	4.67 (3.63 to 6.22)	2.94 (2.76 to 4.10)		

48H	2.55 (2.22 to 3.14)	3.37 (2.22 to 3.78)		
54H	2.76 (2.42 to 3.11)	2.36 (1.75 to 3.69)		
68H	1.60 (1.05 to 1.83)	2.86 (1.59 to 3.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Brain

End point title	Brain
End point description: The brain was only within the PET-field of view for the first 20H.	
End point type	Secondary
End point timeframe: 1 - 68H post tracer injection.	

End point values	Pre-treatment	Post-treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1H	0.11 (0.05 to 0.20)	0.20 (0.18 to 0.24)		
2H	0.06 (0.05 to 0.11)	0.19 (0.11 to 0.34)		
6H	0.13 (0.07 to 0.18)	0.26 (0.18 to 0.31)		
20H	0.12 (0.08 to 0.20)	0.09 (0.07 to 0.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Blood

End point title	Blood
End point description:	
End point type	Secondary
End point timeframe: 1 - 68H post tracer injection.	

End point values	Pre-treatment	Post-treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: kBq/ml				
median (inter-quartile range (Q1-Q3))				
1H	0.86 (0.71 to 0.94)	5.53 (4.46 to 5.91)		
2H	0.69 (0.57 to 0.77)	5.03 (4.01 to 5.32)		
6H	0.44 (0.37 to 0.49)	2.35 (1.98 to 3.16)		
20H	0.34 (0.31 to 0.39)	0.73 (0.59 to 0.99)		
48H	0.35 (0.32 to 0.41)	0.52 (0.49 to 0.55)		
54H	0.28 (0.28 to 0.35)	0.41 (0.38 to 0.44)		
68H	0.28 (0.25 to 0.33)	0.39 (0.36 to 0.46)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events were reported from inclusion into the study (prior to initiation of experimental treatment) and until 2 weeks following final day of treatment.

Adverse event reporting additional description:

No adverse events were reported during the study period or at follow-up.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	None
-----------------	------

Dictionary version	0
--------------------	---

Reporting groups

Reporting group title	Overall
-----------------------	---------

Reporting group description:

No adverse events were reported by any subject in this study.

Participants received a paper form on which they were instructed to report any adverse event, even if they were not sure an event was related to the study. Participants were asked prior to each scan and were contacted by telephone 2 weeks after end-of-treatment.

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4 (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 events reported by participants in this study.

Patients were instructed to note any possible adverse events even if not sure. Participants were provided a paper form in which all adverse events could be filled out and were asked prior to each scan. Participants were contacted by phone 14 days after end-of-treatment and were again asked about any adverse events.

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

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/38081365>