Clinical trial results:
Efficacy of ALXN1840 on human hepatic copper uptake quantified with 64CuCl2 PET/CT-scan.

Summary

EudraCT number	2020-005832-31
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-HV-Cu-Absorption

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,, 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	04 July 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 the effect of ALXN1840 on hepatic copper uptake in healthy participants, compared to the effect of penicillamine, trientine and placebo.

Protection of trial subjects:

Blood samples before and after treatment, including liver, kidney and hematological parameters. Only inclusion of healthy persons 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	01 February 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: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	29
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited through posts in local news papers and social media.

Pre-assignment

Screening details:

Interested persons were contacted by phone and informed about the trial, written participant information was given by mail.
An in-person meeting was conducted for inclusion into the study and evaluation of health status.

Period 1

Period 1 title	Pre-treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The tetrathiomolybdate and placebo groups were double blinded.
The Trientine and Penicillamine groups were not blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Trientine

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cuprior
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg morning, 225 mg evening.

Arm title	Penicillamine

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Metalcaptase
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg morning and 600 mg evening

Arm title	Tetrathiomolybdate

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tetrathiomolybdate
Investigational medicinal product code	
Other name	ALXN1840, bis-choline tetrathiomolybdate, WTX101
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg once daily

Arm title	Placebo

Arm description:

Placebo which was visually identical to tetrathiomolybdate.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet pr day. Visually identical to tetrathiomolybdate.

Number of subjects in period 1	Trientine	Penicillamine	Tetrathiomolybdate
Started	8	8	8
Completed	8	8	8

Number of subjects in period 1	Placebo
Started	8
Completed	8

Period 2

Period 2 title	Post-treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The tetrathiomolybdate and placebo groups were double blinded.
The Trientine and Penicillamine groups were not blinded.

Arms

Are arms mutually exclusive?	Yes

Arm title	Trientine
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Cuprior
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 300 mg morning, 225 mg evening.	
Arm title	Penicillamine
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Metalcaptase
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 600 mg morning and 600 mg evening	
Arm title	Tetrathiomolybdate
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tetrathiomolybdate
Investigational medicinal product code	
Other name	ALXN1840, bis-choline tetrathiomolybdate, WTX101
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 15 mg once daily	
Arm title	Placebo
Arm description: Placebo which was visually identical to tetrathiomolybdate.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 tablet pr day. Visually identical to tetrathiomolybdate.	

Number of subjects in period 2	Trientine	Penicillamine	Tetrathiomolybdate
Started	8	8	8
Completed	8	8	8

Number of subjects in period 2	Placebo
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	Trientine
Reporting group description: -	
Reporting group title	Penicillamine
Reporting group description: -	
Reporting group title	Tetrathiomolybdate
Reporting group description: -	
Reporting group title	Placebo
Reporting group description:	
Placebo which was visually identical to tetrathiomolybdate.	

Reporting group values	Trientine	Penicillamine	Tetrathiomolybdate
Number of subjects	8	8	8
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)	8	8	7
From 65-84 years	0	0	1
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	4	4
Male	4	4	4
Alanine aminotransferase Units: U/L			
median	22.50	24.00	17.50
inter-quartile range (Q1-Q3)	18.00 to 28.00	19.50 to 32.00	13.00 to 26.00
Bilirubin Units: umol/L			
median	11.00	13.00	8.50
inter-quartile range (Q1-Q3)	9.00 to 20.00	11.00 to 14.50	7.50 to 12.50
Creatinine Units: umol/L			
median	64.00	74.50	72.00
inter-quartile range (Q1-Q3)	58.50 to 68.00	61.50 to 78.00	58.50 to 86.50
Serum copper Units: umol/L			
median	17.50	16.05	16.20
inter-quartile range (Q1-Q3)	15.80 to 23.60	14.95 to 25.50	13.40 to 19.15

Reporting group values	Placebo	Total	
Number of subjects	8	32	
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)	6	29	
From 65-84 years	2	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	6	18	
Male	2	14	
Alanine aminotransferase Units: U/L			
median	20.00		
inter-quartile range (Q1-Q3)	17.50 to 29.00	-	
Bilirubin Units: umol/L			
median	11.00		
inter-quartile range (Q1-Q3)	8.50 to 13.00	-	
Creatinine Units: umol/L			
median	70.50		
inter-quartile range (Q1-Q3)	67.50 to 75.50	-	
Serum copper Units: umol/L			
median	14.90		
inter-quartile range (Q1-Q3)	11.90 to 16.40	-	

End points

End points reporting groups	
Reporting group title	Trientine
Reporting group description: -	
Reporting group title	Penicillamine
Reporting group description: -	
Reporting group title	Tetrathiomolybdate
Reporting group description: -	
Reporting group title	Placebo
Reporting group description:	
Placebo which was visually identical to tetrathiomolybdate.	
Reporting group title	Trientine
Reporting group description: -	
Reporting group title	Penicillamine
Reporting group description: -	
Reporting group title	Tetrathiomolybdate
Reporting group description: -	
Reporting group title	Placebo
Reporting group description:	
Placebo which was visually identical to tetrathiomolybdate.	

Primary: Liver SUV	
End point title	Liver SUV
End point description:	
Two scans (1H and 15H) after tracer ingestion. Subjects acted as their own controls. A change in liver SUV was taken as a reduction in intestinal 64copper uptake.	
End point type	Primary
End point timeframe:	
1-15H after tracer ingestion	

End point values	Trientine	Penicillamine	Tetrathiomolybdate	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	8
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1h	6.17 (3.82 to 8.54)	8.78 (5.43 to 10.73)	7.42 (5.56 to 8.19)	6.31 (5.20 to 8.99)
15h	14.24 (13.02 to 16.11)	16.30 (13.55 to 19.18)	13.22 (11.57 to 16.46)	13.62 (11.86 to 15.47)

End point values	Trientine	Penicillamine	Tetrathiomolybdate	Placebo

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	8
Units: SUV				
median (inter-quartile range (Q1-Q3))				
1h	1.47 (1.17 to 4.13)	6.85 (5.81 to 7.71)	0.48 (0.15 to 0.94)	6.12 (5.06 to 9.80)
15h	6.19 (5.24 to 8.67)	12.17 (11.65 to 13.09)	3.05 (1.18 to 5.69)	15.91 (11.70 to 17.94)

Statistical analyses

Statistical analysis title	Tetrathiomolybdate
Comparison groups	Tetrathiomolybdate v Tetrathiomolybdate
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0117 [1]
Method	Sign test

Notes:

[1] - p-value < 0.05 at both 1h and 15h timepoint.

Statistical analysis title	Placebo
Comparison groups	Placebo v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1 [2]
Method	Sign test

Notes:

[2] - p-value > 0.05 at both 1h and 15h timepoint.

Statistical analysis title	Trientine
Comparison groups	Trientine v Trientine
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0117 [3]
Method	Sign test

Notes:

[3] - p-value < 0.05 at both 1h and 15h timepoint.

Statistical analysis title	Penicillamine
Comparison groups	Penicillamine v Penicillamine

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1614 [4]
Method	Sign test

Notes:

[4] - p-value > 0.05 at 1h timepoint.
p-value < 0.05 (0.0357) at 15h timepoint.

Secondary: Blood

End point title	Blood

End point description:

End point type	Secondary

End point timeframe:

1-15H after tracer ingestion.

End point values	Trientine	Penicillamine	Tetrathiomolybdate	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	8
Units: kBq/ml				
median (inter-quartile range (Q1-Q3))				
1h	0.23 (0.06 to 0.38)	0.35 (0.19 to 0.47)	0.44 (0.25 to 0.57)	0.45 (0.19 to 0.56)
15h	0.70 (0.55 to 0.76)	0.62 (0.39 to 0.69)	0.49 (0.44 to 0.57)	0.55 (0.42 to 0.62)

End point values	Trientine	Penicillamine	Tetrathiomolybdate	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	8
Units: kBq/ml				
median (inter-quartile range (Q1-Q3))				
1h	0.05 (0.03 to 0.19)	0.38 (0.24 to 0.51)	0.05 (0.05 to 0.09)	0.26 (0.18 to 0.49)
15h	0.33 (0.21 to 0.45)	0.60 (0.45 to 0.75)	0.29 (0.14 to 0.63)	0.54 (0.37 to 0.60)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from inclusion into the study (prior to initiation of treatment) and until 2 weeks following final day of treatment.	
Adverse event reporting additional description:	
Reporting adverse events possibly related to treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	Trientine
Reporting group description: -	
Reporting group title	Penicillamine
Reporting group description: -	
Reporting group title	Tetrathiomolybdate
Reporting group description: -	
Reporting group title	Placebo
Reporting group description:	
Placebo which was visually identical to tetrathiomolybdate.	

Serious adverse events	Trientine	Penicillamine	Tetrathiomolybdate
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

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

Non-serious adverse events	Trientine	Penicillamine	Tetrathiomolybdate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)	0 / 8 (0.00%)	4 / 8 (50.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	4 / 8 (50.00%)
occurrences (all)	1	0	4
Sleep difficulties			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Minor change in biochemical values			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Gastrointestinal discomfort			
subjects affected / exposed	3 / 8 (37.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Sleep difficulties			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Minor change in biochemical values			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Gastrointestinal discomfort			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

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.

Small sample size and use of healthy individuals.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38088886

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