



## Clinical trial results:

### A Phase 2, Open-label Study to Assess Copper and Molybdenum Balance in Participants With Wilson Disease Treated With ALXN1840 Summary

EudraCT number	2020-001104-41
Trial protocol	GB
Global end of trial date	07 June 2022

#### Results information

Result version number	v1 (current)
This version publication date	23 August 2023
First version publication date	23 August 2023

#### Trial information

##### Trial identification

Sponsor protocol code	ALXN1840-WD-204
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04573309
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Alexion Pharmaceuticals, Inc.
Sponsor organisation address	100 College Street, New Haven, CT, United States, 06510
Public contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals Inc., +33 7 87148158, clinicaltrials.eu@alexion.com
Scientific contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals, Inc., +33 7 87148158, clinicaltrials.eu@alexion.com

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	13 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 June 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to assess net copper balance with daily repeat-dose ALXN1840 treatment (15 mg and 30 mg) in participants with Wilson disease.

Protection of trial subjects:

This trial was conducted in compliance with Good Clinical Practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2020
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	United Kingdom: 6
Country: Number of subjects enrolled	New Zealand: 3
Worldwide total number of subjects	9
EEA total number of subjects	0

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)	9
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study started on 07 Sep 2020 and completed on 07 Jun 2022.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Cohort 1

Arm description:

Participants who had received Wilson disease therapy for >28 days prior to enrollment were administered ALXN1840 at a dose of 15 milligrams (mg)/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.

Arm type	Experimental
Investigational medicinal product name	ALXN1840
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received ALXN1840 at prespecified time points.

<b>Arm title</b>	Cohort 2
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Arm description:

Participants who had received Wilson disease therapy for ≤28 days were administered ALXN1840 at a dose of 15 milligrams/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.

Arm type	Experimental
Investigational medicinal product name	ALXN1840
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received ALXN1840 at prespecified time points.

<b>Number of subjects in period 1</b>	Cohort 1	Cohort 2
Started	8	1
Received at least 1 dose of study drug	8	1
Completed	7	1
Not completed	1	0
Protocol deviation	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

Participants who had received Wilson disease therapy for >28 days prior to enrollment were administered ALXN1840 at a dose of 15 milligrams (mg)/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.

Reporting group title	Cohort 2
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Reporting group description:

Participants who had received Wilson disease therapy for ≤28 days were administered ALXN1840 at a dose of 15 milligrams/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	8	1	9
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	1	9
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.			
Units: years			
arithmetic mean	35.1	26.0	
standard deviation	± 12.41	± 99999	-
Sex: Female, Male			
Units: participants			
Female	1	1	2
Male	7	0	7

## End points

### End points reporting groups

Reporting group title	Cohort 1
Reporting group description: Participants who had received Wilson disease therapy for >28 days prior to enrollment were administered ALXN1840 at a dose of 15 milligrams (mg)/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.	
Reporting group title	Cohort 2
Reporting group description: Participants who had received Wilson disease therapy for ≤28 days were administered ALXN1840 at a dose of 15 milligrams/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.	

### Primary: Mean Daily Copper Balance: Day 1 through Day 8

End point title	Mean Daily Copper Balance: Day 1 through Day 8 <sup>[1]</sup>
End point description: Copper balance is defined as the difference between the measured copper input in food and drink, and the measured copper elimination in urine and feces, and was calculated as the average daily copper balance over the collection period. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.	
End point type	Primary
End point timeframe: Accumulation: Day 1 through Day 8 (ALXN1840 15 mg)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only Descriptive analysis was planned to be reported for this endpoint.	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams/day				
arithmetic mean (standard deviation)	0.8025 (± 0.26860)	0.3062 (± 99999)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Mean Daily Copper Balance: Day 31 through Day 35

End point title	Mean Daily Copper Balance: Day 31 through Day 35 <sup>[2]</sup>
End point description: Copper balance is defined as the difference between the measured copper input in food and drink, and the measured copper elimination in urine and feces, and was calculated as the average daily copper balance over the collection period. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.	

End point type	Primary
End point timeframe:	
Accumulation: Day 31 through Day 35 (ALXN1840 30 mg)	
Notes:	
[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: Only Descriptive analysis was planned to be reported for this endpoint.	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	1		
Units: milligrams/day				
arithmetic mean (standard deviation)	0.9156 ( $\pm$ 0.37982)	0.6613 ( $\pm$ 99999)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Mean Daily Copper Balance: Day 25 through Day 28

End point title	Mean Daily Copper Balance: Day 25 through Day 28 <sup>[3]</sup>
End point description:	
Copper balance is defined as the difference between the measured copper input in food and drink, and the measured copper elimination in urine and feces, and was calculated as the average daily copper balance over the collection period. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.	
End point type	Primary
End point timeframe:	
Accumulation: Day 25 through Day 28 (ALXN1840 15 mg)	
Notes:	
[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: Only Descriptive analysis was planned to be reported for this endpoint.	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	1		
Units: milligrams/day				
arithmetic mean (standard deviation)	0.7109 ( $\pm$ 0.67915)	0.7072 ( $\pm$ 99999)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Mean Daily Copper Balance: Day 36 through Day 39

End point title	Mean Daily Copper Balance: Day 36 through Day 39 <sup>[4]</sup>
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End point description:

Copper balance is defined as the difference between the measured copper input in food and drink, and the measured copper elimination in urine and feces, and was calculated as the average daily copper balance over the collection period. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Primary
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End point timeframe:

Accumulation: Day 36 through Day 39 (ALXN1840 30 mg)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only Descriptive analysis was planned to be reported for this endpoint.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	1		
Units: milligrams/day				
arithmetic mean (standard deviation)	0.9975 (± 0.26543)	0.5662 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline In Mean Daily Copper Balance

End point title	Change From Baseline In Mean Daily Copper Balance
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End point description:

Copper balance is defined as the difference between the measured copper input in food and drink, and the measured copper elimination in urine and feces, and was calculated as the average daily copper balance over the collection period. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Secondary
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End point timeframe:

Accumulation: Baseline, Day 1 through Day 8 (ALXN1840 15 mg) and Day 31 through Day 35 (ALXN1840 30 mg); Steady State: Baseline, Day 25 through Day 28 (ALXN1840 15 mg) and Day 36 through Day 39 (ALXN1840 30 mg)

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams/day				
arithmetic mean (standard deviation)				
Day 1 through Day 8	-0.3780 (± 0.14822)	-0.2060 (± 99999)		
Day 25 through Day 28	-0.4697 (± 0.55770)	0.1950 (± 99999)		



Day 31 through Day 35	-0.2650 ( $\pm$ 0.47135)	0.1492 ( $\pm$ 99999)		
Day 36 through Day 39	-0.1831 ( $\pm$ 0.44589)	0.0540 ( $\pm$ 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Copper Quantified In Food, Drink, Feces, And Urine, Including Plasma Total And Labile Bound Copper (LBC)

End point title	Copper Quantified In Food, Drink, Feces, And Urine, Including Plasma Total And Labile Bound Copper (LBC)
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End point description:

Copper was assessed through measurement of copper intake (in food and drink), and copper output (in feces and urine) as well as plasma total and labile bound copper. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Secondary
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End point timeframe:

Accumulation: Day 1 through Day 8 for 15 mg and Day 31 through Day 35 for 30 mg; Steady state: Day 25 through Day 28 for ALXN1840 15 mg and Day 36 through Day 39 for ALXN1840 30 mg

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams				
arithmetic mean (standard deviation)				
Copper Food Content: Day 1 through Day 8	1.6423 ( $\pm$ 0.15638)	1.3523 ( $\pm$ 99999)		
Copper Food Content: Day 25 through Day 28	1.8269 ( $\pm$ 0.42485)	1.5637 ( $\pm$ 99999)		
Copper Food Content: Day 31 through Day 35	1.8938 ( $\pm$ 0.21846)	1.6022 ( $\pm$ 99999)		
Copper Food Content: Day 36 through Day 39	1.7850 ( $\pm$ 0.20107)	1.4397 ( $\pm$ 99999)		
Copper Drink Content: Day 1 through Day 8	0.0061 ( $\pm$ 0.00159)	0.0055 ( $\pm$ 99999)		
Copper Drink Content: Day 25 through Day 28	0.0066 ( $\pm$ 0.00180)	0.0080 ( $\pm$ 99999)		
Copper Drink Content: Day 31 through Day 35	0.0071 ( $\pm$ 0.00184)	0.0044 ( $\pm$ 99999)		
Copper Drink Content: Day 36 through Day 39	0.0118 ( $\pm$ 0.00920)	0.0045 ( $\pm$ 99999)		
Copper Feces Content: Day 1 through Day 8	0.7594 ( $\pm$ 0.21993)	0.7718 ( $\pm$ 99999)		
Copper Feces Content: Day 25 through Day 28	0.9373 ( $\pm$ 0.30688)	0.7238 ( $\pm$ 99999)		
Copper Feces Content: Day 31 through Day 35	0.8270 ( $\pm$ 0.33746)	0.8720 ( $\pm$ 99999)		
Copper Feces Content: Day 36 through Day 39	0.6136 ( $\pm$ 0.27213)	0.7787 ( $\pm$ 99999)		

Copper Urine Content: Day 1 through Day 8	0.0865 (± 0.05689)	0.2798 (± 99999)		
Copper Urine Content: Day 25 through Day 28	0.1852 (± 0.09079)	0.1408 (± 99999)		
Copper Urine Content: Day 31 through Day 35	0.1584 (± 0.07823)	0.0732 (± 99999)		
Copper Urine Content: Day 36 through Day 39	0.1857 (± 0.09506)	0.0994 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Molybdenum Specified In ALXN1840 Doses Given And Quantified In Food, Drink, Feces, And Urine, Including Plasma At Steady State

End point title	Molybdenum Specified In ALXN1840 Doses Given And Quantified In Food, Drink, Feces, And Urine, Including Plasma At Steady State
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End point description:

Molybdenum balance is defined as the difference between the measured molybdenum intake (in food, drink, and ALXN1840), and molybdenum output (in feces and urine), and was calculated as the average daily molybdenum balance over the collection period. Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Secondary
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End point timeframe:

Day 25 through Day 28 (ALXN1840 15 mg) and Day 36 through Day 39 (ALXN1840 30 mg)

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams				
arithmetic mean (standard deviation)				
Molybdenum Food Content : Days 25 through 28	0.3324 (± 0.18039)	0.3905 (± 99999)		
Molybdenum Food Content : Days 36 through 39	0.1923 (± 0.02354)	0.1724 (± 99999)		
Molybdenum Drink Content : Days 25 through 28	0.0006 (± 0.00012)	0.0018 (± 99999)		
Molybdenum Drink Content : Days 36 through 39	0.0007 (± 0.00024)	0.0004 (± 99999)		
Molybdenum Feces Content : Days 25 through 28	1.1004 (± 0.38506)	1.0656 (± 99999)		
Molybdenum Feces Content : Days 36 through 39	1.0541 (± 0.83207)	2.1352 (± 99999)		
Molybdenum Urine Content : Days 25 through 28	0.7250 (± 0.32736)	0.5480 (± 99999)		
Molybdenum Urine Content : Days 36 through 39	0.8984 (± 0.62633)	1.0395 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline In Total Molybdenum Excretion In Urine And Feces

End point title	Change From Baseline In Total Molybdenum Excretion In Urine And Feces
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End point description:

Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Secondary
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End point timeframe:

Accumulation: Baseline, Day 1 through Day 8 (ALXN1840 15 mg) and Day 31 through Day 35 (ALXN1840 30 mg); Steady State: Baseline, Day 25 through Day 28 (ALXN1840 15 mg) and Day 36 through Day 39 (ALXN1840 30 mg)

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams				
arithmetic mean (standard deviation)				
Molybdenum Feces Content : Day 1 through 8	0.7102 (± 0.22072)	0.9510 (± 99999)		
Molybdenum Feces Content : Days 25 through 28	1.0146 (± 0.42658)	0.9736 (± 99999)		
Molybdenum Feces Content : Days 31 through 35	1.0484 (± 0.62291)	1.7188 (± 99999)		
Molybdenum Feces Content : Days 36 through 39	0.9683 (± 0.88027)	2.0432 (± 99999)		
Molybdenum Urine Content : Day 1 through 8	0.3972 (± 0.15972)	0.1725 (± 99999)		
Molybdenum Urine Content : Days 25 through 28	0.6122 (± 0.28154)	0.4010 (± 99999)		
Molybdenum Urine Content : Days 31 through 35	0.7974 (± 0.47607)	0.8085 (± 99999)		
Molybdenum Urine Content : Days 36 through 39	0.7855 (± 0.58820)	0.8926 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Daily Molybdenum Balance At ALXN1840 Steady State

End point title	Mean Daily Molybdenum Balance At ALXN1840 Steady State
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End point description:

Molybdenum balance at steady state was assessed through measurement of molybdenum intake (in food, drink, and ALXN1840), and molybdenum output (in feces and urine). Steady state is defined as molybdenum (out) equal to molybdenum (in). Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Secondary
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End point timeframe:

Steady state: Day 25 through Day 28 (ALXN1840 15 mg) and Day 36 through Day 39 (ALXN1840 30 mg)

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams				
arithmetic mean (standard deviation)				
Days 25 through 28	1.3618 (± 0.44254)	2.1087 (± 99999)		
Days 36 through 39	2.7599 (± 1.68008)	3.6581 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation Of Molybdenum As Determined By Molybdenum Balance

End point title	Accumulation Of Molybdenum As Determined By Molybdenum Balance
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End point description:

Molybdenum balance was assessed through measurement of molybdenum intake (in food, drink, and ALXN1840), and molybdenum output (in feces and urine). Full analysis set included all participants who received at least 1 dose of ALXN1840 treatment. Here, Number of Participants analyzed signifies those who were evaluable for this outcome measure. 99999 signifies that standard deviation could not be calculated as there was only 1 evaluable participant.

End point type	Secondary
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End point timeframe:

Accumulation: Day 1 through Day 8 (ALXN1840 15 mg) and Day 31 through Day 35 ((ALXN1840 30 mg)

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: milligrams				
arithmetic mean (standard deviation)				
Days 1 through 8	2.2458 (± 0.23232)	2.0876 (± 99999)		
Days 31 through 35	2.6265 (± 1.96365)	4.0775 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Plasma Concentration (Cmax) of Total Molybdenum and Plasma Ultrafiltrate (PUF) Molybdenum

End point title	Maximum Observed Plasma Concentration (Cmax) of Total Molybdenum and Plasma Ultrafiltrate (PUF) Molybdenum
End point description: Pharmacokinetic (PK) analysis set included all participants who had sufficient plasma samples to enable the calculation of PK parameters and provide PK profiles. 99999 signifies that Geometric Coefficient of Variation (CV) could not be calculated as there was only 1 evaluable participant.	
End point type	Secondary
End point timeframe: Day 1 up to Day 39	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: nanograms/milliliters				
geometric mean (geometric coefficient of variation)				
Total Molydenum	430.451 (± 46.6)	1271.551 (± 99999)		
Plasma ultrafiltrate molybdenum	13.546 (± 43.5)	17.823 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under The Concentration Time Curve (AUC0-inf) of Total Molybdenum and Plasma Ultrafiltrate (PUF) Molybdenum

End point title	Area Under The Concentration Time Curve (AUC0-inf) of Total Molybdenum and Plasma Ultrafiltrate (PUF) Molybdenum
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**End point description:**

Pharmacokinetic analysis set included all participants who had sufficient plasma samples to enable the calculation of PK parameters and provide PK profiles. Here, Number of participants analyzed signifies those who were evaluable for this outcome measure and number analyzed signifies those who were evaluable at specified time points. 99999 signifies that geometric CV could not be calculated as there was only 1 evaluable participant.

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End point type	Secondary
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**End point timeframe:**

Day 39

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End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	1		
Units: hours*nanograms/milliliters				
geometric mean (geometric coefficient of variation)				
Total Molybdenum (n=6,1)	13532.591 (± 49.3)	65694.679 (± 99999)		
Plasma ultrafiltrate molybdenum (n=5,1)	292.737 (± 11.9)	476.960 (± 99999)		

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**Statistical analyses**

No statistical analyses for this end point

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## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 56

Adverse event reporting additional description:

Safety set included all participants who received at least 1 dose of ALXN1840.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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### Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

Participants who had received Wilson disease therapy for >28 days prior to enrollment were administered ALXN1840 at a dose of 15 mg/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.

Reporting group title	Cohort 2
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Reporting group description:

Participants who had received Wilson disease therapy for ≤28 days were administered ALXN1840 at a dose of 15 mg/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	1 / 1 (100.00%)	
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nail injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Phlebitis superficial			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	2	
Migraine			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 8 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	2	1	
Abdominal distension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Dry skin			



subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	
Infections and infestations Hordeolum subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	
Periodontitis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	
Pulpitis dental subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 August 2020	The main reason for preparation of this amendment was to update procedures outlined in the Schedule of Activities, remove contradictory text on the reporting of serious adverse events, and add details of an interim analysis.
19 March 2021	The main reason for preparation of this amendment was to revise the exclusion criterion for a urine drug screen. Changes implemented via Administrative Letter 1 and Administrative Letter 2, as well as COVID vaccination guidance, have also been incorporated.
31 August 2021	The main reason for preparation of this amendment was to update the washout period for zinc.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported