Clinical trial results:
A Multicenter, Randomized, Controlled, Open-label, Rater-blinded Study to Evaluate Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of ALXN1840 versus Standard of Care in Pediatric Participants with Wilson Disease

Summary

EudraCT number	2021-001015-82
Trial protocol	DE FR ES PL
Global end of trial date	26 June 2023

Results information

Result version number	v2 (current)
This version publication date	22 September 2024
First version publication date	07 January 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	ALXN1840-WD-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05047523
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Inc.
Sponsor organisation address	121 Seaport Boulevard, Boston, MA, United States, 02210
Public contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc., +33 147100606, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc., +33 147100606, clinicaltrials.eu@alexion.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002232-PIP02-19
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2023
Global end of trial reached?	Yes
Global end of trial date	26 June 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of ALXN1840 administered for 48 weeks, compared to standard of care (SoC), on copper control in participants with Wilson disease (WD) aged 3 to < 18 years of age at the time of enrollment.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines; • Applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines; • Applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 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	Spain: 13
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Australia: 4
Worldwide total number of subjects	40
EEA total number of subjects	24

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)	18
Adolescents (12-17 years)	22
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study consisted of 2 periods: Primary Evaluation Period (PEP) and Open-label Extension (OLE) Period. Participants who completed the 48-week PEP were offered the opportunity to continue treatment in an up to 24-week OLE Period.

Pre-assignment

Screening details:

Per prespecified analysis, participants were randomized, stratified by cohort, in 1:1 ratio to ALXN1840 or continued treatment with Standard of Care (SoC) in Cohort 1 or Cohort 2 for PEP. Stratification was not applicable to OLE Period. Data was collected for the OLE by dose received irrespective of the cohort assigned during randomization.

Period 1

Period 1 title	Primary Evaluation Period (48 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: ALXN1840

Arm description:

Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.

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:

ALXN1840 was administered per schedule specified in the arm description.

Arm title	Cohort 1: SoC Therapy

Arm description:

Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) continued to receive SoC therapy according to the local package label for up to 48 weeks in the PEP.

Arm type	Active comparator
Investigational medicinal product name	SoC Therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

SoC therapy was administered per schedule specified in the arm description.

Arm title	Cohort 2: ALXN1840

Arm description:

Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.

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:

ALXN1840 was administered per schedule specified in the arm description.

Arm title	Cohort 2: SoC Therapy

Arm description:

Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received SoC therapy according to the local package label for up to 48 weeks in the PEP.

Arm type	Active comparator
Investigational medicinal product name	SoC Therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

SoC therapy was administered per schedule specified in the arm description.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This Warning is appearing here due to the limitations of the database. The blinded roles are consistent with this type of study.

Number of subjects in period 1	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840
Started	15	16	4
Received at least 1 dose of study drug	15	16	4
Completed	12	11	0
Not completed	3	5	4
Consent withdrawn by subject	-	1	-
Physician decision	-	-	1
Adverse event, non-fatal	1	-	-
Study Terminated by Sponsor	2	4	3

Number of subjects in period 1	Cohort 2: SoC Therapy
Started	5
Received at least 1 dose of study drug	5
Completed	1
Not completed	4
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-
Study Terminated by Sponsor	4

Period 2

Period 2 title	Extension Period (24 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	ALXN1840/ALXN1840

Arm description:

Participants who were randomized to the ALXN1840 group during the PEP and who completed the 48-week PEP were offered the opportunity to participate in the OLE Period and continued to receive ALXN1840 for up to 24 additional weeks.

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:

ALXN1840 was administered per schedule specified in the arm description.

Arm title	SoC Therapy/ALXN1840

Arm description:

Participants who were randomized to the SoC group during the PEP and who completed the 48-week PEP were offered the opportunity to participate in the OLE Period and received ALXN1840 for up to 24 additional weeks.

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

Dosage and administration details:

ALXN1840 was administered per schedule specified in the arm description.

Number of subjects in period 2	ALXN1840/ALXN1840	SoC Therapy/ALXN1840
Started	12	12
Received at least 1 dose of study drug	12	12
Completed	3	3
Not completed	9	9
Adverse event, non-fatal	1	1
Study Terminated by Sponsor	8	8

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: ALXN1840
Reporting group description:	
Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.	
Reporting group title	Cohort 1: SoC Therapy
Reporting group description:	
Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) continued to receive SoC therapy according to the local package label for up to 48 weeks in the PEP.	
Reporting group title	Cohort 2: ALXN1840
Reporting group description:	
Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.	
Reporting group title	Cohort 2: SoC Therapy
Reporting group description:	
Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received SoC therapy according to the local package label for up to 48 weeks in the PEP.	

Reporting group values	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840
Number of subjects	15	16	4
Age Categorical Units: Subjects			
Children (2-11 years)	6	6	3
Adolescents (12-17 years)	9	10	1
Age Continuous Units: years			
arithmetic mean	11.6	12.8	9.0
standard deviation	± 4.10	± 2.79	± 5.42
Gender Categorical Units: Subjects			
Female	5	4	3
Male	10	12	1
Race Units: Subjects			
Asian	5	6	1
White	9	9	0
Other	1	0	2
Not Reported	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	5	4	0
Not Hispanic or Latino	10	11	4
Not Reported	0	1	0

Reporting group values	Cohort 2: SoC Therapy	Total	
Number of subjects	5	40	

Age Categorical Units: Subjects			
Children (2-11 years)	3	18	
Adolescents (12-17 years)	2	22	
Age Continuous Units: years			
arithmetic mean	10.0		
standard deviation	± 4.36	-	
Gender Categorical Units: Subjects			
Female	3	15	
Male	2	25	
Race Units: Subjects			
Asian	3	15	
White	2	20	
Other	0	3	
Not Reported	0	2	
Ethnicity Units: Subjects			
Hispanic or Latino	0	9	
Not Hispanic or Latino	5	30	
Not Reported	0	1	

End points

End points reporting groups

Reporting group title	Cohort 1: ALXN1840
Reporting group description:	
Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.	
Reporting group title	Cohort 1: SoC Therapy
Reporting group description:	
Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) continued to receive SoC therapy according to the local package label for up to 48 weeks in the PEP.	
Reporting group title	Cohort 2: ALXN1840
Reporting group description:	
Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.	
Reporting group title	Cohort 2: SoC Therapy
Reporting group description:	
Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received SoC therapy according to the local package label for up to 48 weeks in the PEP.	
Reporting group title	ALXN1840/ALXN1840
Reporting group description:	
Participants who were randomized to the ALXN1840 group during the PEP and who completed the 48-week PEP were offered the opportunity to participate in the OLE Period and continued to receive ALXN1840 for up to 24 additional weeks.	
Reporting group title	SoC Therapy/ALXN1840
Reporting group description:	
Participants who were randomized to the SoC group during the PEP and who completed the 48-week PEP were offered the opportunity to participate in the OLE Period and received ALXN1840 for up to 24 additional weeks.	

Primary: Percent Change From Baseline to Week 48 in Non-ceruloplasmin-bound Copper (NCC) in Plasma

End point title	Percent Change From Baseline to Week 48 in Non-ceruloplasmin-bound Copper (NCC) in Plasma[1]
End point description:	
Due to early termination of study, this endpoint was not analyzed.	
End point type	Primary
End point timeframe:	
Baseline, Week 48	

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: The trial was ended early due to discontinuation of the development program. The primary endpoint was not analyzed.

End point values	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840	Cohort 2: SoC Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: percent change				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[2] - Due to early termination of study, this endpoint was not analyzed.

[3] - Due to early termination of study, this endpoint was not analyzed.

[4] - Due to early termination of study, this endpoint was not analyzed.

[5] - Due to early termination of study, this endpoint was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Effect Versus Time Curve (AUEC) for Plasma Total Copper and Direct NCC

End point title	Area Under the Effect Versus Time Curve (AUEC) for Plasma Total Copper and Direct NCC

End point description:

PD analysis set included all participants who had sufficient plasma samples to enable the calculation of PK parameters and provide PK/PD profiles. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. '99999' signifies 'data could not be calculated due to single participant'.

End point type	Secondary

End point timeframe:

Week 48

End point values	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840	Cohort 2: SoC Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	11	0[6]	1
Units: nanograms (ng)*hours (hr)/milliliter(mL)				
arithmetic mean (standard deviation)				
Total Copper	6342.909 (± 3038.3317)	7528.864 (± 4167.2110)	()	16369.000 (± 99999)
Direct NCC	3882.473 (± 1716.4565)	3067.864 (± 1524.9183)	()	4214.000 (± 99999)

Notes:

[6] - No participant was evaluable for this endpoint at specified timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) During the Primary Evaluation Period

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) During the Primary Evaluation Period

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant administered the study drug and which did not necessarily have a causal relationship with this treatment. TEAEs were defined as AEs with onset after the first dose of study intervention or existing events that worsened in severity after the first dose of study intervention. A summary of all Serious Adverse Events and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety analysis set included all participants who received at least 1 dose of ALXN1840 or SoC treatment.

End point type	Secondary

End point timeframe:

Baseline up to Week 48

End point values	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840	Cohort 2: SoC Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	16	4	5
Units: participants	13	13	3	4

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) of ALXN1840 for Plasma Total Molybdenum and Plasma Ultrafiltrate Molybdenum Concentrations

End point title	Maximum Observed Concentration (Cmax) of ALXN1840 for Plasma Total Molybdenum and Plasma Ultrafiltrate Molybdenum Concentrations

End point description:

PK analysis set included all participants who had sufficient plasma samples to enable the calculation of PK parameters and provide PK/PD profiles. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. '99999' signifies 'data could not be calculated due to single participant'.

End point type	Secondary

End point timeframe:

Week 48

End point values	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840	Cohort 2: SoC Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	0[7]	1
Units: ng/milliliters (mL)				
arithmetic mean (standard deviation)				
Plasma Total Molybdenum	183.150 (± 110.4736)	209.355 (± 114.3741)	()	307.000 (± 99999)
Plasma Ultrafiltrate Molybdenum	13.733 (± 8.6186)	17.708 (± 27.9548)	()	9.910 (± 99999)

Notes:

[7] - No participant was evaluable for this endpoint at specified timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the End of the Dosing Interval (AUCtau) of ALXN1840 for Plasma Total Molybdenum and Plasma Ultrafiltrate Molybdenum

End point title	Area Under the Plasma Concentration Versus Time Curve From Time 0 to the End of the Dosing Interval (AUCtau) of ALXN1840 for Plasma Total Molybdenum and Plasma Ultrafiltrate Molybdenum

End point description:

PK analysis set included all participants who had sufficient plasma samples to enable the calculation of PK parameters and provide PK/PD profiles. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. '99999' signifies 'data could not be calculated due to single participant'.

End point type	Secondary

End point timeframe:

Week 48

End point values	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	Cohort 2: ALXN1840	Cohort 2: SoC Therapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	11	0[8]	1
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Plasma Total Molybdenum	4498.082 (± 3054.8300)	2931.045 (± 1694.3512)	()	4261.100 (± 99999)
Plasma Ultrafiltrate Molybdenum	233.154 (± 145.7960)	144.627 (± 88.6710)	()	129.370 (± 99999)

Notes:

[8] - No participant was evaluable for this endpoint at specified timepoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 76

Adverse event reporting additional description:

Safety analysis set included all participants who received at least 1 dose of ALXN1840 or SoC treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Cohort 1: ALXN1840

Reporting group description:

Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.

Reporting group title	Cohort 1: SoC Therapy

Reporting group description:

Participants in Cohort 1 (who received SoC therapy, that is, chelation therapy with penicillamine or trientine, zinc therapy, or a combination of both chelation and zinc therapy for >28 days) continued to receive SoC therapy according to the local package label for up to 48 weeks in the PEP.

Reporting group title	SoC Therapy/ALXN1840

Reporting group description:

Participants who were randomized to the SoC group during the PEP and who completed the 48-week PEP were offered the opportunity to participate in the OLE Period and received ALXN1840 for up to 24 additional weeks.

Reporting group title	Cohort 2: SoC Therapy

Reporting group description:

Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received SoC therapy according to the local package label for up to 48 weeks in the PEP.

Reporting group title	ALXN1840/ALXN1840

Reporting group description:

Participants who were randomized to the ALXN1840 group during the PEP and who completed the 48-week PEP were offered the opportunity to participate in the OLE Period and continued to receive ALXN1840 for up to 24 additional weeks.

Reporting group title	Cohort 2: ALXN1840

Reporting group description:

Participants in Cohort 2 (who were treatment naïve or who received SoC therapy for ≤28 days) received titrated doses of ALXN1840 orally for up to 48 weeks in the PEP.

Serious adverse events	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	SoC Therapy/ALXN1840
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Duodenal perforation			

subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2: SoC Therapy	ALXN1840/ALXN1840	Cohort 2: ALXN1840
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Duodenal perforation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1: ALXN1840	Cohort 1: SoC Therapy	SoC Therapy/ALXN1840
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)	12 / 16 (75.00%)	8 / 12 (66.67%)
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			
subjects affected / exposed	6 / 15 (40.00%)	0 / 16 (0.00%)	2 / 12 (16.67%)
occurrences (all)	7	0	2
Blood cholesterol increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Blood triglycerides increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Electrocardiogram abnormal			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 15 (13.33%)	1 / 16 (6.25%)	2 / 12 (16.67%)
occurrences (all)	2	1	3
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 15 (20.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences (all)	5	0	1
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Nausea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Aphthous ulcer			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Cough			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Rash			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	3 / 16 (18.75%)	0 / 12 (0.00%)
occurrences (all)	1	4	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	3 / 16 (18.75%)	4 / 12 (33.33%)
occurrences (all)	2	3	5
Gastroenteritis			
subjects affected / exposed	2 / 15 (13.33%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
COVID-19			
subjects affected / exposed	6 / 15 (40.00%)	4 / 16 (25.00%)	0 / 12 (0.00%)
occurrences (all)	6	4	0
Gastrointestinal infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Influenza			

subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2

Non-serious adverse events	Cohort 2: SoC Therapy	ALXN1840/ALXN1840	Cohort 2: ALXN1840
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	6 / 12 (50.00%)	2 / 4 (50.00%)
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Blood cholesterol increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	2 / 12 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Hypertransaminasaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Viral infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	2
COVID-19			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2022	The main reason for this amendment was to reduce the maximum daily dose of ALXN1840 from 60 milligrams (mg) for adolescent participants and 30 mg for pediatric participants to 15 mg for all participants.

Notes:

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.

Due to early termination of study, the efficacy endpoints were not analyzed.

Notes: