Clinical trial results:
CHELATE STUDY: Trientine tetrahydrochloride (TETA 4HCl) for the treatment of Wilson's disease

Summary

EudraCT number	2016-003876-29
Trial protocol	DK DE GB AT IT BE
Global end of trial date	18 January 2022

Results information

Result version number	v1 (current)
This version publication date	09 August 2023
First version publication date	09 August 2023

Trial information

Trial identification

Sponsor protocol code	GMPO-131-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03539952
WHO universal trial number (UTN)	-
Other trial identifiers	EudraCT Number: 2016-003876-29

Notes:

Sponsors

Sponsor organisation name	Orphalan SA
Sponsor organisation address	226 Boulevard Voltaire, Paris, France, 75011
Public contact	Clinical Trials Information, Orphalan SA, 33 1 42 49 82 64, naseem.s.amin@orphalan.com
Scientific contact	Clinical Trials Information, Orphalan SA, 33 1 42 49 82 64, naseem.s.amin@orphalan.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	04 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of trientine tetrahydrochloride compared with penicillamine in stable adult Wilson disease patients tolerant to penicillamine. In this non-inferiority randomised trial, the primary endpoint to determine efficacy is the mean difference of non-ceruloplasmin copper (NCC) in serum between the two treatment groups.

Protection of trial subjects:

Home visits were implemented to reduce the intensity of the 4-weekly post-randomization period (week 12-36) compared to 1 to 2 times a year for standard of care visits

Background therapy:

Eligible patients were adults aged between 18 and 75 years receiving penicillamine for at least one year for the treatment of Wilson's disease and on a stable dose for at least 4 months prior to enrolment.

Evidence for comparator:

Comparator:
The other approved chelator, penicillamine, is effective but known to be associated with a high frequency of adverse reactions. It is reported that approximately 30% of Wilson’s disease patients prescribed penicillamine will experience adverse reactions; in the first 1–3 weeks of the treatment, this includes hyper-sensitivity reactions with fever, rash, lymphadenopathy, neutropenia, thrombocytopenia or total aplasia and proteinuria (Sternlieb and Schienberg, 1968), with long-term use associated with side effects including bone marrow toxicity, nephrotoxicity and lupus-like syndrome and dermopathies (Gibbs and Walshe, 1966; Walshe, 1973; Walshe, 1989; Kumagi et al, 2004; Medici et al, 2007; Weiss et al, 2011).

Actual start date of recruitment	09 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Brazil: 17

Worldwide total number of subjects	77
EEA total number of subjects	54

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)	73
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited by selected WD centers. The randomization target was set at 55. Recruitment took place over a period of almost 2 years and ended December 2019

Pre-assignment

Screening details:

WD patients who are considered to be stable by the site investigator, on their standard-of-care penicillamine chelation therapy for at least 1 year, are eligible and once eligible for the study, will enter a 12-week Penicillamine Baseline Period comprising of 1 month (4 weeks) run-in period followed by a 2 month (8 weeks) evaluation period.

Pre-assignment period milestones

Number of subjects started	77
Number of subjects completed	77

Period 1

Period 1 title	Screen and baseline run-in period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Adjudication to confirm baseline egilibility before randomization were blinded to subject nummer and site number

Arms

Arm title	Screen and run-in failures

Arm description:

All subject that were screened, and failed to meet the enrolment criteria between screening and randomization

Arm type	Baseline run-in
Investigational medicinal product name	Penicillamine
Investigational medicinal product code	
Other name	D-penicillamine
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The total daily dose in milligrams of penicillamine to be administered from Day 1 onwards is the same total daily dose in milligrams as the patient’s maintenance dose of penicillamine prior to enrolment in the study.
From Day 1 onwards, the total daily dose is to be administered as two divided doses (BID). If the dose does not divide equally then the higher number of capsules should be taken at the first administration of the day.

Number of subjects in period 1	Screen and run-in failures
Started	77
Completed	53
Not completed	24
Eligibility criteria not met	17
Consent withdrawn by subject	4
Physician decision	1
Lost to follow-up	2

Period 2

Period 2 title	Post randomization phase W12-W36
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Penicillamine arm

Arm description:

All patients in the penicillamine arm will receive following treatments:
Period 1: penicillamine
Period 2: penicillamine
Period 3: penicillamine
Period 4: TETA 4HCl

Arm type	Active comparator
Investigational medicinal product name	Penicillamine
Investigational medicinal product code	
Other name	D-penicillamine
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient will receive its individual daily dose , given as twice daily

Arm title	Trientine tetrahydrochloride arm

Arm description:

All patients in the trientine tetrahydrochloride arm will receive following treatments:
Period 1: penicillamine
Period 2: TETA 4HCl
Period 3: TETA 4HCl
Period 4: TETA 4HCl

Arm type	Experimental
Investigational medicinal product name	TETA 4HCl
Investigational medicinal product code	
Other name	trientien tetrahydrochloride, Cuprior
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The total daily dose in milligrams of trientine base has been the same total daily dose in milligrams of

penicillamine administered at the end of the Penicillamine Baseline Period at Week 12, rounded to the nearest 150 mg of trientine base. Each patient will receive its individual daily dose, given as twice daily

Number of subjects in period 2	Penicillamine arm	Trientine tetrahydrochloride arm
Started	27	26
Completed	26	26
Not completed	1	0
Consent withdrawn by subject	1	-

Period 3	
Period 3 title	1st Extension phase W36-60
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Penicillamine arm

Arm description:

All patients in the penicillamine arm will receive following treatments:
Period 1: penicillamine
Period 2: penicillamine
Period 3: penicillamine
Period 4: TETA 4HCl

Arm type	Active comparator
Investigational medicinal product name	Penicillamine
Investigational medicinal product code	
Other name	D-penicillamine
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient will receive its individual daily dose , given as twice daily

Arm title	Trientine tetrahydrochloride arm

Arm description:

All patients in the trientine tetrahydrochloride arm will receive following treatments:
Period 1: penicillamine
Period 2: TETA 4HCl
Period 3: TETA 4HCl
Period 4: TETA 4HCl

Arm type	Experimental

Investigational medicinal product name	TETA 4HCl
Investigational medicinal product code	
Other name	trientine tetrahydrochloride, Cuprior
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The total daily dose in milligrams of trientine base was the same total daily dose in milligrams of penicillamine administered at the end of the Penicillamine Baseline Period at Week 12, rounded to the nearest 150 mg of trientine base. Each patient will receive its individual daily dose, given as twice daily

Number of subjects in period 3	Penicillamine arm	Trientine tetrahydrochloride arm
Started	26	26
Completed	19	23
Not completed	7	3
Consent withdrawn by subject	3	1
Adverse event, non-fatal	1	1
Other: not further specified	3	1

Period 4

Period 4 title	2nd Extension phase W60 ≤ W108
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Penicillamine arm

Arm description:

All patients in the penicillamine arm will receive following treatments:
Period 1: penicillamine
Period 2: penicillamine
Period 3: penicillamine
Period 4: TETA 4HCl

Arm type	Active comparator
Investigational medicinal product name	TETA 4HCl
Investigational medicinal product code	
Other name	trientine tetrahydrochloride, Cuprior
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The total daily dose in milligrams of trientine base to be administered will be the same total daily dose in milligrams of penicillamine administered at the end of the Penicillamine previous Period at Week 60, rounded to the nearest 150 mg of trientine base. Each patient will receive its individual daily dose, given as twice daily

Arm title	Trientine tetrahydrochloride arm

Arm description:

All patients in the trientine tetrahydrochloride arm will receive following treatments:
Period 1: penicillamine
Period 2: TETA 4HCl
Period 3: TETA 4HCl
Period 4: TETA 4HCl

Arm type	Experimental
Investigational medicinal product name	TETA 4HCl
Investigational medicinal product code	
Other name	trientine tetrahydrochloride, Cuprior
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each patient will receive its individual daily dose , given as twice daily

Number of subjects in period 4	Penicillamine arm	Trientine tetrahydrochloride arm
Started	19	23
Completed	19	21
Not completed	0	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups

Reporting group title	Screen and baseline run-in period

Reporting group description: -

Reporting group values	Screen and baseline run-in period	Total	
Number of subjects	77	77	
Age categorical			
Age was defined to be between 18 and 75 years (extremes included), at the time of consent			
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)	73	73	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	42.9		
standard deviation	± 14.50	-	
Gender categorical			
Units: Subjects			
Female	38	38	
Male	39	39	

Subject analysis sets

Subject analysis set title	Penicillamine arm
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects randomized to Penicillamine treatment

Subject analysis set title	Trientine tetrahydrochloride arm
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects randomized to TETA 4HCl treatment

Reporting group values	Penicillamine arm	Trientine tetrahydrochloride arm	
Number of subjects	27	26	
Age categorical			
Age was defined to be between 18 and 75 years (extremes included), at the time of consent			
Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	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)	51		
From 65-84 years	2		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	43.6		
standard deviation	± 14.49	±	
Gender categorical			
Units: Subjects			
Female	28		
Male	25		

End points

End points reporting groups

Reporting group title	Screen and run-in failures

Reporting group description:

All subject that were screened, and failed to meet the enrolment criteria between screening and randomization

Reporting group title	Penicillamine arm

Reporting group description:

All patients in the penicillamine arm will receive following treatments:
Period 1: penicillamine
Period 2: penicillamine
Period 3: penicillamine
Period 4: TETA 4HCl

Reporting group title	Trientine tetrahydrochloride arm

Reporting group description:

All patients in the trientine tetrahydrochloride arm will receive following treatments:
Period 1: penicillamine
Period 2: TETA 4HCl
Period 3: TETA 4HCl
Period 4: TETA 4HCl

Reporting group title	Penicillamine arm

Reporting group description:

All patients in the penicillamine arm will receive following treatments:
Period 1: penicillamine
Period 2: penicillamine
Period 3: penicillamine
Period 4: TETA 4HCl

Reporting group title	Trientine tetrahydrochloride arm

Reporting group description:

All patients in the trientine tetrahydrochloride arm will receive following treatments:
Period 1: penicillamine
Period 2: TETA 4HCl
Period 3: TETA 4HCl
Period 4: TETA 4HCl

Reporting group title	Penicillamine arm

Reporting group description:

All patients in the penicillamine arm will receive following treatments:
Period 1: penicillamine
Period 2: penicillamine
Period 3: penicillamine
Period 4: TETA 4HCl

Reporting group title	Trientine tetrahydrochloride arm

Reporting group description:

All patients in the trientine tetrahydrochloride arm will receive following treatments:
Period 1: penicillamine
Period 2: TETA 4HCl
Period 3: TETA 4HCl
Period 4: TETA 4HCl

Subject analysis set title	Penicillamine arm
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects randomized to Penicillamine treatment

Subject analysis set title	Trientine tetrahydrochloride arm
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects randomized to TETA 4HCl treatment

Primary: Serum Non-ceruloplasmin bound copper (NCC) concentration

End point title	Serum Non-ceruloplasmin bound copper (NCC) concentration
End point description: Summary statistics	
End point type	Primary
End point timeframe: Week 36	

End point values	Penicillamine arm	Trientine tetrahydrochloride arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: µg/L				
arithmetic mean (standard deviation)	46.5 (± 5.69)	58.7 (± 5.54)		

Statistical analyses

Statistical analysis title	Serum NCC Concentration
Statistical analysis description: The primary endpoint was the assessment of the non-inferiority of TETA 4HCl in relation to D-penicillamine. The non-inferiority assessment was made on the basis of the mean serum NCC level at Week 36	
Comparison groups	Penicillamine arm v Trientine tetrahydrochloride arm
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Mean difference (net)
Point estimate	-9.2
Confidence interval	
level	95 %
sides	1-sided
lower limit	-50
Variability estimate	Standard error of the mean
Dispersion value	7.49

Notes:

[1] - The primary efficacy analysis utilized the serum NCC values from all study visits that were analyzed up to week 36 using a restricted maximum likelihood based general linear model for correlated data. The correlation due to repeated measures was modeled by specifying the variance covariance matrix. Considering a comparison of means in both treatment arms (D-penicillamine minus TETA 4HCl) at the 1-sided 2.5% level of Type 1 error, a noninferiority margin of 50 µg/L was used

Secondary: 24-hour Urinary Copper Excretion (UCE)

End point title	24-hour Urinary Copper Excretion (UCE)
End point description: 24-hour urinary copper excretion (µg/ 24 hr) from urine collected by the patient over a 24-hour period, at week 12 (end of Baseline) and at week 36 (end of period 2, post randomization)	
End point type	Secondary

End point timeframe:
Week 36

End point values	Penicillamine arm	Trientine tetrahydrochloride arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: µg/24 hours				
arithmetic mean (standard deviation)	510.8 (± 47.77)	274.5 (± 45.59)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

To allow for a direct comparission between treatments, only treatment emergent adverse events from week 12 to 36 and from week 36 to 60 are reported.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Penicillamine arm (W12-36)

Reporting group description:

WD patients that were adequately controlled and tolerating penicillamine at the end of the baseline period and being randomized to the penicillamine arm to continue in the 24 week post randomization phase (period 1) on penicillamine. Only (S)AEs reported during the 24 post randomization phase are reflected

Reporting group title	TETA 4HCl arm (W12-36)

Reporting group description:

WD patients that were adequately controlled and tolerating penicillamine at the end of the baseline period and being randomized to the TETA 4HCl arm to continue in the 24 week post randomization phase (period 1) on TETA 4HCl. Only (S)AEs reported during the 24 post randomization phase are reflected

Reporting group title	Penicillamine arm (W36-60)

Reporting group description:

WD patients that were adequately controlled and tolerating penicillamine at the end of the 24 week post randomization phase (period 1) on penicillamine continued on the same treatment in the 1st extension after the post randomization phase (period 1), i.e., penicillamine. Only (S)AEs reported during the 1st extension (W36-60) are reflected

Reporting group title	TETA 4HCl arm (W36-60)

Reporting group description:

WD patients that were adequately controlled and tolerating TETA 4HCl at the end of the 24 week post randomization phase (period 1) continued on the same treatment in the 1st extension after the post randomization phase (period 1), i.e., TETA 4HCl. Only (S)AEs reported during the 1st extension (W36-60) are reflected.

Serious adverse events	Penicillamine arm (W12-36)	TETA 4HCl arm (W12-36)	Penicillamine arm (W36-60)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 27 (11.11%)	0 / 26 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholangiocarcinoma			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cancer			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TETA 4HCl arm (W36-60)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholangiocarcinoma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cancer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukopenia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Penicillamine arm (W12-36)	TETA 4HCl arm (W12-36)	Penicillamine arm (W36-60)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 27 (33.33%)	6 / 26 (23.08%)	3 / 24 (12.50%)
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 27 (3.70%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Injury, poisoning and procedural complications			
Fall			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 27 (18.52%)	2 / 26 (7.69%)	1 / 24 (4.17%)
occurrences (all)	8	4	1
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			

Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 27 (3.70%)	4 / 26 (15.38%)	0 / 24 (0.00%)
occurrences (all)	1	12	0
Abnormal faeces			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	3	0
Dry mouth			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 27 (3.70%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 27 (3.70%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Renal and urinary disorders			
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Psychiatric disorders			
Mood swings			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 27 (11.11%)	1 / 26 (3.85%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Infections and infestations			
Gastroenteritis viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	0 / 24 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	TETA 4HCl arm (W36-60)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)		
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

Abdominal pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Abnormal faeces alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Dry mouth alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Constipation alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Skin and subcutaneous tissue disorders Alopecia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Renal and urinary disorders Urinary tract infection alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Psychiatric disorders Mood swings alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Infections and infestations Gastroenteritis viral alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 0 / 25 (0.00%) 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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36183738