



Clinical trial results:

A Phase I Pharmacokinetic Profiling Study in Patients Receiving Trientine Dihydrochloride for the Treatment of Wilson's Disease

Summary

EudraCT number	2012-004445-32
Trial protocol	DE
Global end of trial date	06 March 2014

Results information

Result version number	v1 (current)
This version publication date	18 February 2016
First version publication date	18 February 2016

Trial information

Trial identification

Sponsor protocol code	TR-001PK
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Univar BV
Sponsor organisation address	Bramley Road, Milton Keynes, United Kingdom, MK1 1PT
Public contact	Trientine Enquiries, Univar BV, +44 0845202 6401, Trientine@univareurope.com
Scientific contact	Trientine Enquiries, Univar BV, +44 0845202 6401, Trientine@univareurope.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	06 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 March 2014
Global end of trial reached?	Yes
Global end of trial date	06 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetics of a single dose of trientine in children ≥ 6 years and adult patients with Wilson's disease by pharmacokinetic (PK) analysis.

Protection of trial subjects:

Participation in the study was voluntary and subject to the required patient information and consent procedures. The PIS clearly explained the trial procedures if he/she was to take part. All trial participants were existing Wilson Disease patients, who were used to the need for blood draws as part of their care. IP administered on Day 1 was the patients' usual prescribed dose. All patients received close care and monitoring for the duration of the study and beyond in line with their routine treatment plan.

Background therapy:

Background therapy not applicable.

Evidence for comparator:

Comparator(s) not applicable.

Actual start date of recruitment	04 June 2013
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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	4
Adults (18-64 years)	16

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pre-screening processes were in place for all patients who did and did not visit the site regularly for the PI to select eligible patients who were to be invited to participate in the study.

Pre-assignment

Screening details:

Principle screening criteria were patients with confirmed Wilson disease (Leipzig score > 3), aged ≥ 6 years, whose current treatment was trientine dihydrochloride.

Period 1

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

Arms

Arm title	Trientine dihydrochloride 300mg
Arm description: -	
Arm type	Profiling arm
Investigational medicinal product name	Trientine dihydrochloride 300mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Patients took their usual prescribed dose (1 dose to be taken on the morning of the study visit).

Number of subjects in period 1	Trientine dihydrochloride 300mg
Started	20
Completed	20

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	4	4	
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	
Adults (18-64 years)	16	16	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	9	9	

End points

End points reporting groups

Reporting group title	Trientine dihydrochloride 300mg
Reporting group description: -	

Primary: Maximum plasma drug concentration level (C_{max}) and normalised for dose (C_{max}/D)

End point title	Maximum plasma drug concentration level (C _{max}) and normalised for dose (C _{max} /D) ^[1]
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End point description:

The maximum plasma concentration (C_{max}) for each subject was derived directly from their plasma concentration-time profiles. Dose-normalised parameters were generated by dividing the C_{max} and the area under the plasma concentration time curve from zero to the last quantifiable concentration in the profile (AUC 0-t) by the nominal dose of trientine dihydrochloride received by the subject.

End point type	Primary
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End point timeframe:

Sampling pre-dose (30 mins before drug intake), then at 30 mins, 1, 1.5, 2, 3, 4, 5, 6, 8, 12 h post dose

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 object of the study was to determine Pharmacokinetic variables

End point values	Trientine dihydrochloride 300mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng/mL				
arithmetic mean (standard deviation)				
C _{max}	1274.9 (± 707.27)			
C _{max} /D	1.937 (± 1.0801)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to maximum plasma concentration (T_{max}) and terminal elimination half-life (t_{1/2})

End point title	Time to maximum plasma concentration (T _{max}) and terminal elimination half-life (t _{1/2}) ^[2]
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End point description:

The time to maximum plasma drug concentration was derived directly from the patient's plasma concentration-time profile.

The t_{1/2} is calculated from the equation $t_{1/2} = 0.693 / \lambda_z$ (λ_z = terminal elimination rate constant).

End point type	Primary
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End point timeframe:

Sampling pre-dose (30 mins before drug intake), then 30 mins, 1, 1.5, 2, 3, 4, 5, 6, 8, 12 h post dose

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: The object of the study was to determine Pharmacokinetic variables

End point values	Trientine dihydrochloride 300mg			
Subject group type	Reporting group			
Number of subjects analysed	20 ^[3]			
Units: hours				
arithmetic mean (standard deviation)				
Tmax	1.738 (± 1.06)			
t½	3.772 (± 1.2775)			

Notes:

[3] - Available observations for Tmax = 20

Available observations for t½ = 14

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUC0-t); Area under the plasma concentration-time curve from zero to infinite time (AUC0-inf); AUC0-t normalised for dose (AUC0-t/D)

End point title	Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUC0-t); Area under the plasma concentration-time curve from zero to infinite time (AUC0-inf); AUC0-t normalised for dose (AUC0-t/D) ^[4]
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End point description:

AUC0-t was calculated by the linear trapezoidal rule between increasing concentrations and the logarithmic trapezoidal rule between decreasing concentrations. A minimum of 3 quantifiable time points in the plasma concentration-time profile were required for generation of the AUC0-t.

AUC0-inf was calculated using the formula $AUC0-t + C_t/\lambda_z$, with C being the last quantifiable plasma concentration in the profile.

AUC0-t/D was calculated by dividing the AUC0-t by the nominal dose of trientine dihydrochloride received by the subject.

End point type	Primary
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End point timeframe:

Sampling pre-dose (30 mins before drug intake), then at 30 mins, 1, 1.5, 2, 3, 4, 5, 6, 8, 12 h post dose.

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: The object of the study was to determine Pharmacokinetic variables

End point values	Trientine dihydrochloride 300mg			
Subject group type	Reporting group			
Number of subjects analysed	20 ^[5]			
Units: ng/mL.h				
arithmetic mean (standard deviation)				
AUC0-t	5075.5 (± 3633.56)			

AUC0-inf	5942.1 ($\pm$ 4054.45)			
AUC0-t/D	7.624 ($\pm$ 4.7302)			

Notes:

[5] - Observations for AUC0-t = 20

Observations for AUC0-inf = 14

Observations for AUC0-t/D = 20

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Overall trial period

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16
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Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Due to the nature and duration of this study, no adverse events (serious or otherwise) were reported.

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