



Clinical trial results:

Plasma kinetics for tablet and liquid formulations of 6-mercaptopurine in childhood acute lymphoblastic leukemia

Summary

EudraCT number	2013-001236-21
Trial protocol	DK
Global end of trial date	27 March 2018

Results information

Result version number	v1 (current)
This version publication date	01 January 2021
First version publication date	01 January 2021

Trial information

Trial identification

Sponsor protocol code	2008-003235-20
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01906671
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Clinical Trial information, Kjeld Schmiegelow, +45 35451357, Kjeld.Schmiegelow@regionh.dk
Scientific contact	Clinical Trial information, Kjeld Schmiegelow, +45 35451357, Kjeld.Schmiegelow@regionh.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2018
Global end of trial reached?	Yes
Global end of trial date	27 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to investigate whether previous findings, from a trial conducted on healthy adults regarding plasma kinetics and bioavailability of tablet (Puri-Nethol) and oral liquid formulation (Xaluprine) of 6-mercaptopurine, is similar in the target population, children with ALL.

Protection of trial subjects:

Patients were examined in a well known and safe environment, and ingested 6-mercaptopurine, which is part of their normal treatment for acute lymphoblastic leukemia

Background therapy:

Children diagnosed with acute lymphoblastic leukemia are treated according to the Nordic Society of Pediatric Hematology and Oncology (NOPHO) ALL2008 protocol, where 6-mercaptopurine comprises one of two cornerstones of maintenance therapy. In this trial we aimed to compare pharmacokinetics of tablet and liquid formulations of 6-mercaptopurine, which is thus a normal part of these children's treatment.

Evidence for comparator:

A comparative pharmacokinetic study in healthy adults demonstrated bioequivalence between tablet and liquid formulation of 6-mercaptopurine, we aimed to explore this in the target population, children with acute lymphoblastic leukemia

Actual start date of recruitment	24 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	Denmark: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	16

Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Clinical examination, and receiving maintenance therapy according to Nordic Society of Pediatric Hematology and Oncology (NOPHO) ALL2008 protocol

Pre-assignment

Screening details:

Clinical examination

Receiving maintenance therapy according to the NOPHO ALL2008 protocol

Period 1

Period 1 title	Purinethol
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Purinethol (tablet version of 6-mercaptopurine)
Arm description: -	
Arm type	Regular treatment
Investigational medicinal product name	6-mercaptopurine
Investigational medicinal product code	
Other name	Puri-nethol
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

According to the child's therapeutic 6-mercaptopurine dose

Number of subjects in period 1	Purinethol (tablet version of 6-mercaptopurine)
Started	17
Completed	16
Not completed	1
Consent withdrawn by subject	1

Period 2

Period 2 title	Xaluprine
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Xaluprine (liquid formulation of 6-mercaptopurine)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	6-mercaptopurine
Investigational medicinal product code	
Other name	Xaluprine
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

According to the child's therapeutic 6-mercaptopurine dose

Number of subjects in period 2	Xaluprine (liquid formulation of 6-mercaptopurine)
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Purinethol
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Reporting group description: -

Reporting group values	Purinethol	Total	
Number of subjects	17	17	
Age categorical			
Units: Subjects			
Children (2-11 years)	16	16	
Adolescents (12-17 years)	1	1	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	9	9	
Diagnosis of acute lymphoblastoc leukemia			
Units: Subjects			
ALL	17	17	

Subject analysis sets

Subject analysis set title	Full analysis
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Subject analysis set type	Full analysis
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Subject analysis set description:

Full analysis of all pharmacokinetic parameters

Reporting group values	Full analysis		
Number of subjects	16		
Age categorical			
Units: Subjects			
Children (2-11 years)	15		
Adolescents (12-17 years)	1		
Gender categorical			
Units: Subjects			
Female	8		
Male	8		
Diagnosis of acute lymphoblastoc leukemia			
Units: Subjects			
ALL	16		

End points

End points reporting groups

Reporting group title	Purinethol (tablet version of 6-mercaptopurine)
Reporting group description: -	
Reporting group title	Xaluprine (liquid formulation of 6-mercaptopurine)
Reporting group description: -	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis of all pharmacokinetic parameters	

Primary: Pharmacokinetic parameters, AUC, Cmax, Tmax, t_{1/2}

End point title	Pharmacokinetic parameters, AUC, Cmax, Tmax, t _{1/2}
End point description:	
End point type	Primary
End point timeframe:	
On blood samples taken on study days.	

End point values	Purinethol (tablet version of 6- mercaptopurine)	Xaluprine (liquid formulation of 6- mercaptopurine)	Full analysis	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16	
Units: nmol/L				
number (not applicable)	16	16	16	

Statistical analyses

Statistical analysis title	Paired t-tests
Comparison groups	Xaluprine (liquid formulation of 6-mercaptopurine) v Purinethol (tablet version of 6-mercaptopurine)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
lower limit	0.8
upper limit	1.25

<div>Variability estimate</div>	<div>Standard error of the mean</div>
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Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Upon leaving the trial unit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Frequency threshold for reporting non-serious adverse events: 0.01 %

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: As this was a small study, with only 17 participants and a short timeframe, no non-serious adverse events 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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32519032>