Clinical trial results:
Thiopurines with Low Dose Allopurinol: a prospective one way cross-over study

Summary

EudraCT number	2016-001638-84
Trial protocol	NL
Global end of trial date	01 September 2017

Results information

Result version number	v1 (current)
This version publication date	07 January 2020
First version publication date	07 January 2020
Summary attachment (see zip file)	Summary ThiLDA study (abstract) EudraCT (Summary Abstract (EudraCT) ThiLDA study.pdf)

Trial information

Trial identification

Sponsor protocol code	16-07

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Meander medical center
Sponsor organisation address	Maatweg 3, Amersfoort, Netherlands, 3813 TZ
Public contact	SF Chavoushi, Meander Medical Center, 0031 612928800, faraz.chavoushi@gmail.com
Scientific contact	SF Chavoushi, Meander Medical Center, 0031 612928800, faraz.chavoushi@gmail.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	01 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2017
Global end of trial reached?	Yes
Global end of trial date	01 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigating whether 50 mg allopurinol is non-inferior to 100 mg in combination with azathioprine or mercaptopurine by measuring and comparing thiopurine metabolites

Protection of trial subjects:

trial subjects were seen every few weeks (AND during 'regular clinical' follow-up visits)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
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	Netherlands: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

study subjects were recruited by using existing the electronic records database. patients were called, informed and asked to participate (and, before participating, sign an informed consent form)

Pre-assignment

Screening details:

study subjects were recruited by using existing the electronic records database, and by using the inclusion and exclusion criteria

Period 1

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

Blinding implementation details:

none

Arms

Are arms mutually exclusive?	Yes
Arm title	one way crossover group

Arm description:

one way crossover group (22 patients in total group, and in reality there was only ONE arm/group! We had to add two arms in EudraCT because of a million errors that we get due to a faulty website which does not let us proceed with only one arm...)

Arm type	single arm (one way crossover)
Investigational medicinal product name	Allopurinol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg and 50 mg:
at start of the intervention (=switch from 100mg to 50 mg tablets) the 100 mg tablets will be splitted/divided in two pieces by
using a pill splitter and the existing scoring ('dividing') line on the 100 mg tablet

Arm title	one way crossover (same group, total = 22)

Arm description:

one way crossover group (22 patients in total group, and in reality there was only ONE arm/group! We had to add two arms in EudraCT because of a million errors that we get due to a faulty website which does not let us proceed with only one arm...)

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

Dosage and administration details:

100 mg and 50 mg:
at start of the intervention (=switch from 100mg to 50 mg tablets) the 100 mg tablets will be splitted/divided in two pieces by
using a pill splitter and the existing scoring ('dividing') line on the 100 mg tablet

Number of subjects in period 1	one way crossover group	one way crossover (same group, total = 22)
Started	11	11
start	11	11
used allopurinol 50 mg for at least 30d	11	11
finished	11	11
Completed	11	11

Baseline characteristics

Reporting groups	
Reporting group title	control
Reporting group description: one-way crossover group	

Reporting group values	control	Total	
Number of subjects	22	22	
Age categorical Units: Subjects			

Age continuous			
all subjects were >18 years of age			
Units: years			
arithmetic mean	38.3		
standard deviation	± 7	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	11	11	

End points

End points reporting groups

Reporting group title	one way crossover group
Reporting group description:	
one way crossover group (22 patients in total group, and in reality there was only ONE arm/group! We had to add two arms in EudraCT because of a million errors that we get due to a faulty website which does not let us proceed with only one arm...)	
Reporting group title	one way crossover (same group, total = 22)
Reporting group description:	
one way crossover group (22 patients in total group, and in reality there was only ONE arm/group! We had to add two arms in EudraCT because of a million errors that we get due to a faulty website which does not let us proceed with only one arm...)	

Primary: thiopurine metabolite concentrations (6-TGN)

End point title	thiopurine metabolite concentrations (6-TGN)
End point description:	
End point type	Primary
End point timeframe:	
before/after intervention	

End point values	one way crossover group	one way crossover (same group, total = 22)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11[1]		
Units: pmol/8*108 RBC				
arithmetic mean (standard deviation)				
before intervention	761 (± 0)	761 (± 0)		
after intervention	625 (± 0)	625 (± 0)		

Notes:

[1] - 22 patients in total group, and in reality there was only ONE arm/group! (faulty EudraCT website!)

Statistical analyses

Statistical analysis title	metabolite conc statistical analysis
Statistical analysis description:	
paired t-test	
Comparison groups	one way crossover group v one way crossover (same group, total = 22)

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.005
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	-136
Confidence interval	
level	95 %
sides	2-sided
lower limit	-227.5
upper limit	-45.3
Variability estimate	Standard error of the mean
Dispersion value	0

Notes:

[2] - paired t-test

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: during trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	patient's doctor
Dictionary version	1

Reporting groups	
Reporting group title	one way crossover group

Reporting group description:

one way crossover group

Serious adverse events	one way crossover group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	one way crossover group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		

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: 13 patients experienced AEs after intervention. 3 of those subjects experienced fatigue (please see full paper for all reported AEs and further details). Also there were 22 patients in total group, and in reality there was only ONE arm/group! (could not proceed with just one single arm due to faulty EudraCT website!)

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

n/a

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31587102