



## Clinical trial results: Immunomonitoring of tacrolimus in healthy volunteers Summary

EudraCT number	2018-001775-20
Trial protocol	NL
Global end of trial date	21 August 2018

### Results information

Result version number	v1 (current)
This version publication date	23 March 2022
First version publication date	23 March 2022
Summary attachment (see zip file)	M3. CHDR1644_Manuscript_30Jul2019 (M3. CHDR1644_Manuscript_30Jul2019.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	CHDR1644
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Centre for Human Drug Research
Sponsor organisation address	Zernikedreef 8, Leiden, Netherlands, 2333 CL
Public contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	09 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 August 2018
Global end of trial reached?	Yes
Global end of trial date	21 August 2018
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

To investigate the pharmacokinetic profile of a single dose of tacrolimus;

- o Whole blood concentrations
- o Cellular concentrations (T cells and/or PBMCs)
- o Relationship between whole blood and cellular concentrations

To investigate the pharmacodynamic effects of a single dose of tacrolimus;

- o Calcineurin activity
- o T cell function (activation, proliferation)

To investigate the relationship between the pharmacokinetic profile of tacrolimus (in whole blood and intracellular) and the pharmacodynamic effects ex vivo;

To investigate the correlation between pharmacodynamic effects (calcineurin activity and T cell function) in vitro and ex vivo;

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Protection of trial subjects:

No medical benefit was expected from this study for the participating subjects.

The study drug is a registered medicinal product for the prevention of prophylaxis of the transplanted organ in transplantation patients, and has been used before in many healthy volunteer studies. All study drug administrations were done in the clinic under medical supervision. The subjects that received the study drug remained in the clinic for at least 7 hours after the study drug administration for the subjects to be closely monitored for any adverse signs during the treatment.

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Background therapy: -

Evidence for comparator:

No comparator.

Actual start date of recruitment	13 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

Notes:

<b>Subjects enrolled per age group</b>	
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)	12
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Recruitment from 13-Jun2018 – 11-Aug-2018. Location: Netherlands

### Pre-assignment

Screening details:

Healthy male or female subjects, 18-55 years of age (inclusive), without evidence of any active or chronic illness or any clinically significant abnormalities in laboratory test results, ECG and blood pressure.

### Period 1

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

### Arms

<b>Arm title</b>	Healthy volunteers (active)
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Arm description:

Twelve treated subjects (0.05 mg/kg Prograf (Tacrolimus)), no placebo.

Arm type	Experimental
Investigational medicinal product name	Prograf
Investigational medicinal product code	
Other name	Tacrolimus
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A single oral dose of 0.05 mg/kg Prograf (rounded to available dosage forms) with a glass of water.

<b>Number of subjects in period 1</b>	Healthy volunteers (active)
Started	12
Completed	12

## Baseline characteristics

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### Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	12	12	
Age categorical			
Healthy subjects 18-55 years of age			
Units: Subjects			
Adults (18-64 years)	12	12	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	6	6	

## End points

### End points reporting groups

Reporting group title	Healthy volunteers (active)
Reporting group description: Twelve treated subjects (0.05 mg/kg Prograf (Tacrolimus)), no placebo.	

### Primary: Tacrolimus concentration

End point title	Tacrolimus concentration <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe: Pre-dose and 1.5, 48, 96 and 192 hours after drug administration.	

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: See uploaded article for results, endpoints and analyses.

End point values	Healthy volunteers (active)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: microgram(s)/litre				
arithmetic mean (standard deviation)	21.468 ( $\pm$ 6.16)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From screening (up to 42 days pre-dose) until follow-up visit (7 days post-dose).

Adverse event reporting additional description:

Adverse events were investigated by the investigator routinely on all study visits and AE intensity, relationship to study intervention, chronicity and eventual actions related to the AE were determined.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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### Reporting groups

Reporting group title	Active
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Reporting group description:

Subjects treated with 0.05 mg/kg Prograf (tacrolimus)

Serious adverse events	Active		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (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	Active		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)		
Vascular disorders			
Presyncope			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal stiffness subjects affected / exposed occurrences (all)  Myalgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1  1 / 12 (8.33%) 1		



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2018	Increase of blood volume.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31547590>