Clinical trial results:
A randomised controlled comparison of standard release Tacrolimus vs extended-release Tacrolimus as baseline maintenance monotherapy for kidney transplantation after induction with Campath 1-H.

Summary

EudraCT number	2008-000889-22
Trial protocol	GB
Global end of trial date	29 March 2012

Results information

Result version number	v1 (current)
This version publication date	08 February 2020
First version publication date	08 February 2020

Trial information

Trial identification

Sponsor protocol code	ICKTI08TX01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00807144
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College Healthcare NHS Trust
Sponsor organisation address	Pread Street, London, United Kingdom, W2 1NY
Public contact	Adam McLean, Imperial College Healthcare NHS Trust, adammclean@nhs.net
Scientific contact	Adam McLean, Imperial College Healthcare NHS Trust, adammclean@nhs.net

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	16 January 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 March 2012
Global end of trial reached?	Yes
Global end of trial date	29 March 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare outcomes of kidney transplantation after induction with Alemtuzumab/short course steroids, followed by maintenance with either standard release Tacrolimus (Prograf) monotherapy, or extended-release tacrolimus (Advagraf) monotherapy.

Primary outcome measures: Survival with a functioning graft at 1 year and 3 years.

Protection of trial subjects:

None

Background therapy:

Alemtuzumab 30mg IV post-operatively. Early steroid withdrawal with Prednisolone: 3 days 60mg then 4 days 30 mg then steroid cessation.

Evidence for comparator: -

Actual start date of recruitment	02 December 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 102
Worldwide total number of subjects	102
EEA total number of subjects	102

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)	84
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

the recruitment was at Imperial College Kidney & Transplant Centre, Hammersmith Hospital, United Kingdom.

Pre-assignment

Screening details:

Follow the protocol.

Period 1

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

Blinding implementation details:

Open-labelled

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard release tacrolimus

Arm description:

Participants received Standard release Tacrolimus (Prograf) 0.05 mg/kg twice daily

Arm type	Active comparator
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	
Other name	Prograf
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

0.05 mg/kg twice daily

Arm title	Extended Release Tacrolimus

Arm description:

Participants received Tacrolimus 0.1 mg/kg once daily

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

Dosage and administration details:

0.1 mg/kg once daily

Number of subjects in period 1	Standard release tacrolimus	Extended Release Tacrolimus
Started	50	52
Completed	48	52
Not completed	2	0
death	1	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Standard release tacrolimus
Reporting group description:	
Participants received Standard release Tacrolimus (Prograf) 0.05 mg/kg twice daily	

Reporting group title	Extended Release Tacrolimus
Reporting group description:	
Participants received Tacrolimus 0.1 mg/kg once daily	

Reporting group values	Standard release tacrolimus	Extended Release Tacrolimus	Total
Number of subjects	50	52	102
Age categorical Units: Subjects			
Adults (50-70years)	50	52	102
Age continuous Units: years			
arithmetic mean	51.5	53.1	
standard deviation	± 14.4	± 15.8	-
Gender categorical Units: Subjects			
Female	13	13	26
Male	37	39	76

End points

End points reporting groups	
Reporting group title	Standard release tacrolimus
Reporting group description: Participants received Standard release Tacrolimus (Prograf) 0.05 mg/kg twice daily	

Reporting group title	Extended Release Tacrolimus
Reporting group description: Participants received Tacrolimus 0.1 mg/kg once daily	

Primary: Survival with functioning graft	
End point title	Survival with functioning graft
End point description:	
End point type	Primary
End point timeframe: 1 year	

End point values	Standard release tacrolimus	Extended Release Tacrolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: percent				
number (not applicable)	96	92.3		

Statistical analyses

Statistical analysis title	Functioning graft
Comparison groups	Standard release tacrolimus v Extended Release Tacrolimus
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Logrank

Secondary: Rejection-free survival year 1	
End point title	Rejection-free survival year 1
End point description:	

End point type	Secondary
End point timeframe:	
1 year	

End point values	Standard release tacrolimus	Extended Release Tacrolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: percent				
number (not applicable)	84	86		

Statistical analyses

Statistical analysis title	Rejection-free survival
Comparison groups	Standard release tacrolimus v Extended Release Tacrolimus
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	Logrank

Secondary: Rejection-free survival year 2

End point title	Rejection-free survival year 2
End point description:	
End point type	Secondary
End point timeframe:	
2 years	

End point values	Standard release tacrolimus	Extended Release Tacrolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: percent				
number (not applicable)	80.1	83.4		

Statistical analyses

Statistical analysis title	Rejection free survival year 2
Comparison groups	Standard release tacrolimus v Extended Release Tacrolimus
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75
Method	Logrank

Secondary: Mean graft function

End point title	Mean graft function

End point description:

End point type	Secondary

End point timeframe:

1 year

End point values	Standard release tacrolimus	Extended Release Tacrolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: ml/min				
number (confidence interval 95%)	53.9 (47 to 60)	54.0 (46.5 to 61.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2 years	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10
Reporting groups	
Reporting group title	Standard release tacrolimus
Reporting group description: Participants received Standard release Tacrolimus (Prograf) 0.05 mg/kg twice daily	
Reporting group title	Extended Release Tacrolimus
Reporting group description: Participants received Tacrolimus 0.1 mg/kg once daily	

Serious adverse events	Standard release tacrolimus	Extended Release Tacrolimus	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Hepatobiliary disorders			
Liver failure			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Standard release tacrolimus	Extended Release Tacrolimus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 50 (18.00%)	8 / 52 (15.38%)	
General disorders and administration site conditions			
Any rejection symptome			
subjects affected / exposed	9 / 50 (18.00%)	8 / 52 (15.38%)	
occurrences (all)	9	8	

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