Clinical trial results:
A randomised controlled comparison of CampathTacrolimus vs IL2R MoAb Tacrolimus / Mycophenolate as InductionMaintenance immunosuppression in kidney transplantation.

Summary

EudraCT number	2005-002856-17
Trial protocol	GB
Global end of trial date	01 June 2011

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	SMHREN0501

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00246129
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	04 June 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2011
Global end of trial reached?	Yes
Global end of trial date	01 June 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine which of two well established anti−rejection drug combinations has the best outcome in kidney transplantation.
The investigational regime (Regime 1: IL2RMoAb−Tacrolimus/Mycophenolate) uses a combination of a relatively mild intial treatment with more potent long−term therapy, the second (comparator) regime (Regime 2: Campath−Tacrolimus) uses potent inital treatment, with simpler, less potent long−term treatment; this is our current standard baseline immunotherapeutic regime.

Protection of trial subjects:

None

Background therapy:

All patients received 3 months of CMV prophylaxis with 450 mg once daily Valganciclovir initially, adjusted for estimated glomerular filtration rate, and 6 months Pneumocystis prophylaxis with Co-Trimoxazole 480 mg three times per week.
Both groups received a rapid steroid withdrawal regimen (0.5 g IV methyl-prednisolone intra-operatively at the release of vascular clamps with oral prednisolone 1 mg/kg up to max 60 mg on postoperative days 1 to 3 then prednisolone 0.5 mg/kg up to max 30 mg on days 4 to 7 followed by steroid cessation, unless rejection had occurred during the week 1.)

Evidence for comparator: -

Actual start date of recruitment	11 October 2005
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	United Kingdom: 123
Worldwide total number of subjects	123
EEA total number of subjects	123

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	116
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited between 2005 and 2011.

Pre-assignment

Screening details:

The kidney transplant participants were recruiting at the West London Renal and Transplant Centre.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Campath-Tacrolimus

Arm description:

Patients received alemtuzumab induction as a single IV infusion of 30 mg alemtuzumab (MabCampath) on return from theaters with tacrolimus (Prograf, Astellas) monotherapy long-term maintenance. Tacrolimus initially was 0.1 mg/kg in two equally divided doses, adjusted to achieve target 12 hr trough levels of 5 to 8 ng/mL by liquid chromatography/tandem mass spectrometry (equivalent to 6.5–10 ng/mL measured by immunoassay).

Arm type	Experimental
Investigational medicinal product name	Campath
Investigational medicinal product code	
Other name	Alemtuzumab
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients received alemtuzumab induction as a single IV infusion of 30 mg on return from theatre

Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	
Other name	Prograf, Astellas
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Patients received on return from theaters and long-term monotherapy. Initially, 0.1 mg/kg in two equally divided doses, adjusted to achieve target 12 hr trough levels of 5 to 8 ng/mL by liquid chromatography/tandem mass spectrometry (equivalent to 6.5–10 ng/mL measured by immunoassay).

Arm title	Daclizumab-Tacrolimus-Mycophenolate

Arm description:

Patients received daclizumab (Zenapax) induction given as 2x2 mg/kg infusions on return from theaters and on day 14, with combined tacrolimus/mycophenolate mofetil (CellCept) long-term maintenance.

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

Dosage and administration details:	
Initially, 0.15 mg/kg in two divided doses, adjusted to target trough levels of 8 to 12 ng/mL (equivalent to 10 –15 ng/mL).	
Investigational medicinal product name	Mycophenolate mofetil
Investigational medicinal product code	
Other name	Cellcept
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Initially, 500 mg BD adjusted to achieve target 12 hr trough mycophenolic acid levels of 1.5 to 3.0 mg/L.	
Investigational medicinal product name	Daclizumab
Investigational medicinal product code	
Other name	Zenapax
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Induction given as 2x2 mg/kg infusions on return from theaters and on day 14.	

Number of subjects in period 1	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate
Started	82	41
Completed	75	39
Not completed	7	2
death	2	1
suffered primary non-function	1	-
Lost to follow-up	1	-
graft failed	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Campath-Tacrolimus
Reporting group description:	
Patients received alemtuzumab induction as a single IV infusion of 30 mg alemtuzumab (MabCampath) on return from theaters with tacrolimus (Prograf, Astellas) monotherapy long-term maintenance. Tacrolimus initially was 0.1 mg/kg in two equally divided doses, adjusted to achieve target 12 hr trough levels of 5 to 8 ng/mL by liquid chromatography/tandem mass spectrometry (equivalent to 6.5–10 ng/mL measured by immunoassay).	
Reporting group title	Daclizumab-Tacrolimus-Mycophenolate
Reporting group description:	
Patients received daclizumab (Zenapax) induction given as 2x2 mg/kg infusions on return from theaters and on day 14, with combined tacrolimus/mycophenolate mofetil (CellCept) long-term maintenance.	

Reporting group values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate	Total
Number of subjects	82	41	123
Age categorical Units: Subjects			
Adults (18-64 years)	77	39	116
From 65-84 years	5	2	7
Age continuous Units: years			
arithmetic mean	47.3	47.0	
standard deviation	± 13.4	± 10.6	-
Gender categorical Units: Subjects			
Female	28	14	42
Male	54	27	81

End points

End points reporting groups

Reporting group title	Campath-Tacrolimus
Reporting group description:	
Patients received alemtuzumab induction as a single IV infusion of 30 mg alemtuzumab (MabCampath) on return from theaters with tacrolimus (Prograf, Astellas) monotherapy long-term maintenance. Tacrolimus initially was 0.1 mg/kg in two equally divided doses, adjusted to achieve target 12 hr trough levels of 5 to 8 ng/mL by liquid chromatography/tandem mass spectrometry (equivalent to 6.5–10 ng/mL measured by immunoassay).	
Reporting group title	Daclizumab-Tacrolimus-Mycophenolate
Reporting group description:	
Patients received daclizumab (Zenapax) induction given as 2x2 mg/kg infusions on return from theaters and on day 14, with combined tacrolimus/mycophenolate mofetil (CellCept) long-term maintenance.	

Primary: One Year Survival With a Functioning Graft

End point title	One Year Survival With a Functioning Graft
End point description:	
End point type	Primary
End point timeframe:	
1 year	

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: Percent of transplant recipients				
number (confidence interval 90%)	97.6 (90.6 to 99.4)	95.1 (81.9 to 98.8)		

Statistical analyses

Statistical analysis title	Functioning graft
Comparison groups	Campath-Tacrolimus v Daclizumab-Tacrolimus-Mycophenolate
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.467
Method	Logrank

Secondary: Occurrence, Severity, and Type of Rejection Episodes

End point title	Occurrence, Severity, and Type of Rejection Episodes

End point description:

End point type	Secondary

End point timeframe:

1 year

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: Percentage of transplant recipients				
number (confidence interval 90%)	91.2 (82.4 to 95.7)	82.3 (66.4 to 91.1)		

Statistical analyses

Statistical analysis title	Rejection free survival
Comparison groups	Campath-Tacrolimus v Daclizumab-Tacrolimus-Mycophenolate
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.138
Method	Logrank

Secondary: Occurrence, Severity, and Type of Infection Episodes

End point title	Occurrence, Severity, and Type of Infection Episodes

End point description:

End point type	Secondary

End point timeframe:

1 year

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: per 100 patient years				
number (not applicable)	73	76		

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Length of Stay in Hospital

End point title	Initial Length of Stay in Hospital

End point description:

End point type	Secondary

End point timeframe:

1 year

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: day				
arithmetic mean (standard deviation)	11.7 (± 6.4)	12.1 (± 7.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Early Development of Scarring in the Grafts

End point title	Early Development of Scarring in the Grafts

End point description:

End point type	Secondary

End point timeframe:

1 year

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: Percentage of transplant recipients				
number (not applicable)	96	90		

Statistical analyses

No statistical analyses for this end point

Secondary: Graft Function, Creatinin level

End point title	Graft Function, Creatinin level

End point description:

End point type	Secondary

End point timeframe:

2 years

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: mmol/L				
arithmetic mean (standard deviation)	127.3 (± 36.2)	147.0 (± 69.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Survival

End point title	Patient Survival

End point description:

End point type	Secondary

End point timeframe:

2 years

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: Percentage or transplant recipients				
number (not applicable)	98	98		

Statistical analyses

No statistical analyses for this end point

Secondary: Graft Survival Censored for Death With Function

End point title	Graft Survival Censored for Death With Function

End point description:

End point type	Secondary

End point timeframe:

2 years

End point values	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: Percentage or transplant recipients				
number (not applicable)	91	95		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
1 years	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Campath-Tacrolimus
Reporting group description:	
Campath induction with 7-day short-course steroids followed by tacrolimus monotherapy	
Reporting group title	Daclizumab-Tacrolimus-Mycophenolate
Reporting group description:	
Daclizumab induction with 7-day short-course steroids followed by Tacrolimus and Mycophenolate mofetil therapy	

Serious adverse events	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 82 (6.10%)	5 / 41 (12.20%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 82 (1.22%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
New-onset diabetes after transplantation	Additional description: NODAT		
subjects affected / exposed	4 / 82 (4.88%)	5 / 41 (12.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Campath-Tacrolimus	Daclizumab-Tacrolimus-Mycophenolate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 82 (71.95%)	30 / 41 (73.17%)	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	31 / 82 (37.80%)	9 / 41 (21.95%)	
occurrences (all)	31	9	
Bacteraemia			
subjects affected / exposed	15 / 82 (18.29%)	9 / 41 (21.95%)	
occurrences (all)	15	9	
Wound infection			
subjects affected / exposed	6 / 82 (7.32%)	6 / 41 (14.63%)	
occurrences (all)	6	6	
Cytomegalovirus infection			
subjects affected / exposed	1 / 82 (1.22%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
Other			
subjects affected / exposed	6 / 82 (7.32%)	2 / 41 (4.88%)	
occurrences (all)	6	2	

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/21836540