Clinical trial results:
A randomised clinical trial of mycophenolate mofetil versus cyclophosphamide for remission induction in ANCA associated vasculitis

Summary

EudraCT number	2006-001663-33
Trial protocol	GB CZ ES SE DE IT AT FR
Global end of trial date	14 February 2013

Results information

Result version number	v1 (current)
This version publication date	08 July 2016
First version publication date	30 July 2015
Summary attachment (see zip file)	MYCYC serious adverse events (mycyc_sae.pdf)

Trial information

Trial identification

Sponsor protocol code	MYCYC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00414128
WHO universal trial number (UTN)	-
Other trial identifiers	NA: NA

Notes:

Sponsors

Sponsor organisation name	Cambridge University Hospitals NHS Foundation Trust
Sponsor organisation address	Hills Road, Cambridge, United Kingdom, CB2 0QQ
Public contact	David Jayne, Addenbrooke's Hospital , +44 1223 217159, dj106@cam.ac.uk
Scientific contact	David Jayne, Addenbrooke's Hospital , +44 1223 217159, dj106@cam.ac.uk

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 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2013
Global end of trial reached?	Yes
Global end of trial date	14 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this trial was to investigate whether a mycophenolate mofetil based induction regimen is as effective as a cyclophosphamide based induction regimen in the treatment of active ANCA associated vasculitis.

Protection of trial subjects:

All patients were provided with a patient information sheet and provided written informed consent and were free to withdraw from the trial at any point without giving a reason. Patient confidentiality was respected according to national regulations and data was coded before computer entry to maintain confidentiality. Blood samples were coded before being sent to Addenbrooke's Hospital. Study follow up and blood tests were arranged to coincide with standard hospital appointments to avoid additional hospital visits and blood tests as much as possible. According to the trial protocol, patients who did not respond to their assigned treatment regimen, could be withdrawn from trial protocol and treated with additional therapies as required.

Background therapy:

All patients in this trial received oral glucocorticoids. Glucocorticoid starting dose was 1mg/kg/day reducing down gradually to 5mg per day at the end of month 9 for adults and 0.05-0.075mg/kg/day for patients under the age of 17 years and to continue at this dose until study end at 18 months.

Evidence for comparator:

Cyclophosphamide is the 'gold standard' treatment for remission induction in ANCA vasculitis. It was introduced as a therapy for ANCA vasculitis in 1970 and is associated with remission rates of 70-90% and one year survival rates of 80-90% (survival prior to the introduction of cyclophosphamide was 20%).

Actual start date of recruitment	12 March 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	100 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 73
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Australia: 13

Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	New Zealand: 2
Worldwide total number of subjects	140
EEA total number of subjects	125

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)	1
Adolescents (12-17 years)	8
Adults (18-64 years)	86
From 65 to 84 years	42
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Patient were recruited from outpatient clinics and on medical wards. The study was open to recruitment of adults from 31-Jan-2007, with paediatric inclusion from 31-Jul-2007. Last patient was recruited on 29-Jul-2011.

Pre-assignment

Screening details:

All patients were locally screened for eligibility. Randomisation forms were sent to the central site for all patients who were considered eligible by local sites. A total of 154 patients were screened and put forward for randomisation, 14 were excluded (6 did not meet inclusion criteria, 8 declined to participate) and 140 patients were randomise

Period 1

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

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	Cyclophosphamide

Arm description:

Control

Arm type	Control
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	5,00911E+15
Other name	ACT code L01AA01, CAS 50180
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Per day dose, based on weight, age and renal function, 10 doses of a maximum of 1.2g

Arm title	Mycophenolate mofetil

Arm description:

Test

Arm type	Test
Investigational medicinal product name	Cellcept (mycophenolate mofetil)
Investigational medicinal product code	
Other name	MA number EU/1/96/005/002, ACT code L04AA06, CAS 128794-94-5
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosed twice daily. Maximum dose 300mg total per day.

Number of subjects in period 1	Cyclophosphamide	Mycophenolate mofetil
Started	70	70
Completed	70	70

Baseline characteristics

Reporting groups	
Reporting group title	Cyclophosphamide
Reporting group description: Control	
Reporting group title	Mycophenolate mofetil
Reporting group description: Test	

Reporting group values	Cyclophosphamide	Mycophenolate mofetil	Total
Number of subjects	70	70	140
Age categorical			
Whole trial			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	2	2
Adolescents (12-17 years)	4	4	8
Adults (18-64 years)	45	42	87
From 65-84 years	18	22	40
85 years and over	3	0	3
Age continuous			
Whole trial			
Units: years			
median	60.5	59.6	
full range (min-max)	13.5 to 87	9.6 to 81.8	-
Gender categorical			
Whole trial			
Units: Subjects			
Female	37	29	66
Male	33	41	74

End points

End points reporting groups	
Reporting group title	Cyclophosphamide
Reporting group description: Control	
Reporting group title	Mycophenolate mofetil
Reporting group description: Test	

Primary: Absolute Risk Reduction - ARR (90% Confidence Interval)	
End point title	Absolute Risk Reduction - ARR (90% Confidence Interval)
End point description: Number of patients that achieved remission by six months	
End point type	Primary
End point timeframe: Remission by six months	

End point values	Cyclophosphamide	Mycophenolate mofetil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Number	70	70		

Statistical analyses

Statistical analysis title	ITT
Statistical analysis description: ITT	
Comparison groups	Cyclophosphamide v Mycophenolate mofetil
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.05
Method	Absolute Risk Difference
Parameter estimate	Risk difference (RD)
Point estimate	0.057

Confidence interval	
level	90 %
sides	1-sided
lower limit	-0.073

Notes:

[1] - The non-inferiority margin is an absolute risk difference of 12% for remission outcomes

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Serious adverse events reported to trial management committee within 24 hours of occurrence followed by subsequent reporting to the MHRA according to MHRA criteria.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

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

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: Please see the attachment for the serious adverse events. The non-serious adverse events have not yet been analysed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2007	Substantial ammendement to adult protocol (Version 2A) for changes requested by MHRA- drug blood monitoring and changes to mycophenolate mofetil regimen, three additional exclusion criteria added
26 November 2007	Substantial ammendement for paediatric protocol (Version 2P) to MHRA for inclusion of children
04 April 2008	Substantial ammendment for paediatric protocol (Version 3P) changes to paediatric dosing in protocol to allow MCRN study adoption
21 June 2011	Substantial ammendment for adult protocol (Version 3A) PIS and consent forms (Version 4) for updated safety information

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported