Clinical trial results:
An Open Label Randomised Controlled Trial of Mycophenolate Mofetil Versus Cyclophosphamide for the Induction of Remission of Childhood Polyarteritis Nodosa

Summary

EudraCT number	2013-004668-71
Trial protocol	GB IT PT ES BE
Global end of trial date	26 June 2020

Results information

Result version number	v1 (current)
This version publication date	03 January 2021
First version publication date	03 January 2021

Trial information

Trial identification

Sponsor protocol code	11/0499

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	EudraCT: 2013-004668-71

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom,
Public contact	Professor Paul Brogan, University College London, p.brogan@ucl.ac.uk
Scientific contact	Professor Paul Brogan, University College London, p.brogan@ucl.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	24 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Is mycophenelate mofetil (MMF) as effective as cyclophosphamide (CYC) at inducing remission in children with polyarteritis nodosa (PAN)?

Protection of trial subjects:

The identification and recruitment of participants to the MYPAN trial and the administration of the trial treatments was carried out by trained health care professionals in a hospital environment following standard, routine procedures. All those who oversaw treatment were trained on the study, evidenced by the collection of site delegation logs. Current CVs and GCP certificates were also obtained for all staff members who had a delegated duty within the study.

All members of site staff who approached the participant's family for consent were trained on the study and equipped with sufficient knowledge to answer any trial related questions. In addition, these members of staff had the required clinical skills to provide additional support to those families that were emotionally distressed by their child's condition. Patient data was collected at site using CRFs specifically designed for the MYPAN trial. All collected information was pseudo-anonymised and transferred to the Liverpool Clinical Trials Centre (LCTC) in an agreed secure format. The management of the study was done in line with Ethical, Regulatory and LCTC policies/procedures.

Protocol procedures included mechanisms to manage anticipated adverse reactions due to the established safety profiles of the trial interventions. For example, the trial interventions are immunosuppressants that can be associated with opportunistic infection, and mandatory prophylaxis with cotrimoxazole was required to prevent this occurrence. Other examples of risk mitigation were the prescribing of MMF at half the recommended dose for the first week, thereafter increasing to the full dose in order to mitigate against gastrointestinal adverse effects, and the use of anti-emetics and recommended co-administration of MESNA and adequate hydration as standard for CYC allocated participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Turkey: 3
Worldwide total number of subjects	11
EEA total number of subjects	8

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)	8
Adolescents (12-17 years)	3
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

11 subjects were recruited: 7 from the UK (3 sites), 1 from Spain, and 3 from Turkey (1 site). The first subject was randomised on 09/03/2015, and the last on 06/06/2018.
8 participating sites did not recruit.

Pre-assignment

Screening details:

13 subjects were screened. 1 did not meet eligibility criteria, and 1 did not agree to participate.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Mycophenolate mofetil (MMF)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Mycophenolate mofetil
Investigational medicinal product code	24280-93-1
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

For ease of administration, for the tablets and capsules the dose should be rounded to the nearest multiple of 250 (as long as within 10% of target dose).
The 1g/5ml powder should be reconstituted in accordance with the manufacturer's SmPC.
The starting dose is 600 mg/m² per day (maximum 1g per day) for the first week. Thereafter the dose is 1200 mg/m² per day, maximum 2g per day, in two divided doses.
MMF may be stopped from 3 months onward provided patient in remission (PVAS 0 for 2 consecutive study assessments at least 1 month apart). After completion of MMF, AZA to be commenced the next day.
If the target dose is not tolerated, patients should receive the maximum tolerated dose.

Arm title	Intravenous Cyclophosphamide (CYC)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The preparation of CYC should be in accordance with the manufacturer's instructions on intravenous infusion, provided on the relevant SmPC.
MESNA and IV fluids will be administered as per existing local practice.
- CYC is given as intravenous pulses at weeks 0, 2, 4 and then every 3 weeks until remission is reached from start of therapy (max 10 doses, min 6 doses) at a dose of 500-750 mg/m2 (maximum 1.2g).
- The dose is adjusted based on Leukocyte count, hepatic, and renal function according to a standard protocol (see Table 1).
- CYC may be stopped after a minimum of 6 doses (week 13) provided patient in remission (PVAS 0 for 2 consecutive study assessments at least a month (4 weeks) apart and adhering to protocol steroid

taper).

Number of subjects in period 1	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)
Started	6	5
Completed	6	5

Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Mycophenolate mofetil (MMF)

Arm description:

3-6 months (12-24 weeks) induction therapy with oral MMF

Arm type	Experimental
Investigational medicinal product name	Mycophenolate mofetil
Investigational medicinal product code	24280-93-1
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

For ease of administration, for the tablets and capsules the dose should be rounded to the nearest multiple of 250 (as long as within 10% of target dose).
The 1g/5ml powder should be reconstituted in accordance with the manufacturer’s SmPC.
The starting dose is 600 mg/m² per day (maximum 1g per day) for the first week. Thereafter the dose is 1200 mg/m² per day, maximum 2g per day, in two divided doses.
MMF may be stopped from 3 months onward provided patient in remission (PVAS 0 for 2 consecutive study assessments at least 1 month apart). After completion of MMF, AZA to be commenced the next day.
If the target dose is not tolerated, patients should receive the maximum tolerated dose.

Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	Prednisone / Methylprednisolone
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Both groups will receive the same protocolised prednisolone/prednisone starting at 1mg/kg/day weaning to 0.1 mg/kg/day by 6 months (24 weeks)

Arm title	Intravenous Cyclophosphamide (CYC)

Arm description:

3-6 months (12-24 weeks) induction therapy with intravenous CYC regimen

Arm type	Active comparator
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The preparation of CYC should be in accordance with the manufacturer’s instructions on intravenous infusion, provided on the relevant SmPC.
MESNA and IV fluids will be administered as per existing local practice.
- CYC is given as intravenous pulses at weeks 0, 2, 4 and then every 3 weeks until remission is reached from start of therapy (max 10 doses, min 6 doses) at a dose of 500-750 mg/m2 (maximum 1.2g).
- The dose is adjusted based on Leukocyte count, hepatic, and renal function according to a standard protocol (see Table 1).
- CYC may be stopped after a minimum of 6 doses (week 13) provided patient in remission (PVAS 0 for 2 consecutive study assessments at least a month (4 weeks) apart and adhering to protocol steroid taper).

Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	Prednisone / Methylprednisolone
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Both groups will receive the same protocolised prednisolone/prednisone starting at 1mg/kg/day weaning to 0.1 mg/kg/day by 6 months (24 weeks)

Number of subjects in period 2	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)
Started	6	5
Completed	6	5

Period 3

Period 3 title	Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Mycophenolate mofetil (MMF)

Arm description: -

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

Dosage and administration details:

Dose is 2 mg/kg/day, maximum 200 mg/day, rounded to the nearest 25 mg. Weight at time of commencing azathioprine to be used for dose calculation.
- Check FBC and alanine transaminase (ALT) or aspartate transaminase (AST) (for hepatotoxicity):
a. Every two weeks for one month (4 weeks)
b. Every two months (8 weeks) for the first 12 months (48 weeks)
c. Then three-monthly (every 12 weeks)
- Stop if leukocytes <4.0 x 109 cells/l. Restart when leukocytes ≥ 4.0 x109 cells/l with AZA dose reduced by at least 25%. Monitor weekly for one month (4 weeks).
- If liver transaminases are over twice upper limit of normal level then Azathioprine should be temporarily discontinued.
- Thiopurine s-methyltransferase (TPMT) activity or polymorphism assessment to be used according to local practice, but this is not a mandatory requirement.

Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	Prednisone / Methylprednisolone
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.05-0.075 mg/kg by 9 months (36 weeks) and until trial end at 18 months (72 weeks).

Arm title	Intravenous Cyclophosphamide (CYC)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Azathioprine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose is 2 mg/kg/day, maximum 200 mg/day, rounded to the nearest 25 mg. Weight at time of commencing azathioprine to be used for dose calculation.
- Check FBC and alanine transaminase (ALT) or aspartate transaminase (AST) (for hepatotoxicity):
a. Every two weeks for one month (4 weeks)
b. Every two months (8 weeks) for the first 12 months (48 weeks)
c. Then three-monthly (every 12 weeks)
- Stop if leukocytes <4.0 x 109 cells/l. Restart when leukocytes ≥ 4.0 x109 cells/l with AZA dose reduced by at least 25%. Monitor weekly for one month (4 weeks).
- If liver transaminases are over twice upper limit of normal level then Azathioprine should be temporarily discontinued.
- Thiopurine s-methyltransferase (TPMT) activity or polymorphism assessment to be used according to local practice, but this is not a mandatory requirement.

Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	Prednisone / Methylprednisolone
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.05-0.075 mg/kg by 9 months (36 weeks) and until trial end at 18 months (72 weeks).

Number of subjects in period 3	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)
Started	6	5
Completed	5	5
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Mycophenolate mofetil (MMF)
Reporting group description: -	
Reporting group title	Intravenous Cyclophosphamide (CYC)
Reporting group description: -	

Reporting group values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)	Total
Number of subjects	6	5	11
Age categorical 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)	4	4	8
Adolescents (12-17 years)	2	1	3
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	10.8	7.9	
inter-quartile range (Q1-Q3)	7.0 to 12.1	6.7 to 9.4	-
Gender categorical Units: Subjects			
Female	3	3	6
Male	3	2	5

End points

End points reporting groups

Reporting group title	Mycophenolate mofetil (MMF)
Reporting group description: -	
Reporting group title	Intravenous Cyclophosphamide (CYC)
Reporting group description: -	
Reporting group title	Mycophenolate mofetil (MMF)
Reporting group description: 3-6 months (12-24 weeks) induction therapy with oral MMF	
Reporting group title	Intravenous Cyclophosphamide (CYC)
Reporting group description: 3-6 months (12-24 weeks) induction therapy with intravenous CYC regimen	

Reporting group title	Mycophenolate mofetil (MMF)
Reporting group description: -	
Reporting group title	Intravenous Cyclophosphamide (CYC)
Reporting group description: -	

Primary: Remission within 24 weeks with adherence to protocolised corticosteroid taper

End point title	Remission within 24 weeks with adherence to protocolised corticosteroid taper
End point description: Remission within six months (24 weeks) of randomisation defined as a paediatric vasculitis activity score (PVAS) of zero on two consecutive readings (both within 6 months (24 weeks) of randomisation ≥ one month (4 weeks) apart, with adherence to the protocolised corticosteroid taper.	
End point type	Primary
End point timeframe: 24 weeks	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Subjects	4	4		

Statistical analyses

Statistical analysis title	Bayesian analysis
Statistical analysis description: Calculation of a posterior distribution for the probability of remission within 6-months of randomisation to MMF	
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)

Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Probability
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.85

Notes:

[1] - Presentation of summary statistics for the posterior distribution (mode and 95% credible interval)

Statistical analysis title	Bayesian analysis

Statistical analysis description:

Calculation of a posterior distribution for the probability of remission within 6-months of randomisation to CYC

Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Probability
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.87

Notes:

[2] - Presentation of summary statistics for the posterior distribution (mode and 95% credible interval)

Statistical analysis title	Bayesian analysis

Statistical analysis description:

Calculation of a posterior distribution for the odds-ratio of remission within 6-months of randomisation to MMF vs CYC

Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Probability
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.88

Notes:

[3] - Presentation of summary statistics for the posterior distribution (mode and 95% credible interval)

Secondary: Remission within 24 weeks irrespective of adherence to protocolised corticosteroid taper

End point title	Remission within 24 weeks irrespective of adherence to protocolised corticosteroid taper

End point description:

Remission within six months (24 weeks) of randomisation defined as paediatric vasculitis activity score (PVAS) of zero on two consecutive readings ≥ one month (4 weeks) apart, irrespective of adherence to a protocolised corticosteroid taper

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Subjects	4	4		

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

Does treatment arm have a significant effect on remission rates

Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact
Parameter estimate	Relative Risk
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.5

Secondary: Time to remission, with adherence to a protocolised corticosteroid taper

End point title	Time to remission, with adherence to a protocolised corticosteroid taper

End point description:

Time to remission defined as PVAS of zero on two consecutive readings ≥ one month (4 weeks) apart, with adherence to a protocolised corticosteroid taper, measured from randomisation

End point type	Secondary

End point timeframe:

From randomisation to 72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Weeks				
median (confidence interval 95%)	7.1 (4.0 to 999)	17.6 (4.4 to 35.3)		

Attachments (see zip file)	Kaplan-Meier curve showing time to remission/Fig 6-3.png

Statistical analyses

No statistical analyses for this end point

Secondary: Paediatric vasculitis damage index (PVDI) at 24 weeks

End point title	Paediatric vasculitis damage index (PVDI) at 24 weeks

End point description:

Paediatric vasculitis damage index (PVDI – modified from the adult VDI) at 6, 12 and 18 months (24, 48 and 72 weeks) after randomisation

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	0.5 (0 to 1)	2 (0 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Paediatric vasculitis damage index (PVDI) at 48 weeks

End point title	Paediatric vasculitis damage index (PVDI) at 48 weeks

End point description:
Paediatric vasculitis damage index (PVDI – modified from the adult VDI) at 6, 12 and 18 months (24, 48 and 72 weeks) after randomisation

End point type	Secondary

End point timeframe:
48 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	2 (0 to 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Paediatric vasculitis damage index (PVDI) at 72 weeks

End point title	Paediatric vasculitis damage index (PVDI) at 72 weeks

End point description:
Paediatric vasculitis damage index (PVDI – modified from the adult VDI) at 6, 12 and 18 months (24, 48 and 72 weeks) after randomisation

End point type	Secondary

End point timeframe:
72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	2 (0 to 3)		

Attachments (see zip file)	MMF PVDI over time/Fig 6-4a.png CYC PVDI over time/Fig 6-4b.png

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Disability Index at Baseline

End point title	CHAQ Disability Index at Baseline

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

Baseline

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	1.5 (0.6 to 2.4)	1.5 (0.3 to 1.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Disability Index at 16 weeks

End point title	CHAQ Disability Index at 16 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	0.3 (0 to 0.6)	1.0 (0 to 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Disability Index at 24 weeks

End point title	CHAQ Disability Index at 24 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	0.1 (0 to 0.1)	0.5 (0 to 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Disability Index at 48 weeks

End point title	CHAQ Disability Index at 48 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 0.1)	0.8 (0.1 to 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Disability Index at 72 weeks

End point title	CHAQ Disability Index at 72 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	1.0 (0.2 to 1.8)		

Attachments (see zip file)	MMF CHAQ disability Patient Profiles/Fig 6-5a.png CYC CHAQ Disability: Patient Profiles/Fig 6-5b.png

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Pain at Baseline

End point title	CHAQ Pain at Baseline

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

Baseline

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	40.5 (6.0 to 70.5)	30.5 (5.5 to 56.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Pain at 16 weeks

End point title	CHAQ Pain at 16 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	0.5 (0 to 20.5)	2.5 (0 to 27.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Pain at 24 weeks

End point title	CHAQ Pain at 24 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	4.5 (1.0 to 34.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Pain at 48 weeks

End point title	CHAQ Pain at 48 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	2 (0 to 12)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ Pain at 72 weeks

End point title	CHAQ Pain at 72 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general health.

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	2 (0 to 4)		

Attachments (see zip file)	MMF CHAQ Pain: Patient Profiles/Fig 6-6a.png CYC CHAQ Pain: Patient Profiles/Fig 6-6b.png

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ General Evaluation at Baseline

End point title	CHAQ General Evaluation at Baseline

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general evaluation.

End point type	Secondary

End point timeframe:

Baseline

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: Units				
median (inter-quartile range (Q1-Q3))	35 (6 to 68.5)	15 (0 to 79)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ General Evaluation at 16 weeks

End point title	CHAQ General Evaluation at 16 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general evaluation.

End point type	Secondary

End point timeframe:

16 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	8.5 (2.5 to 16)	10 (6 to 11)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ General Evaluation at 24 weeks

End point title	CHAQ General Evaluation at 24 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general evaluation.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	8 (1 to 29.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ General Evaluation at 48 weeks

End point title	CHAQ General Evaluation at 48 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general evaluation.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	5 (0 to 22)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHAQ General Evaluation at 72 weeks

End point title	CHAQ General Evaluation at 72 weeks

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is a functional outcome score measuring disability, pain, and general evaluation.

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Units				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	2 (0 to 4)		

Attachments (see zip file)	MMF CHAQ General Evaluation: Patient Profiles/Fig 6-7a.png CYC CHAQ General Evaluation: Patient Profiles/Fig 6-7b.png

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Physical Summary Score (PhS) at Baseline

End point title	CHQ Physical Summary Score (PhS) at Baseline

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-

scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

Baseline

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	8.3 (-0.4 to 18.0)	9.0 (1.8 to 14.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Physical Summary Score (PhS) at 16 weeks

End point title	CHQ Physical Summary Score (PhS) at 16 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

16 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	42.9 (32.1 to 50.5)	12.8 (6.3 to 35.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Physical Summary Score (PhS) at 24 weeks

End point title	CHQ Physical Summary Score (PhS) at 24 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	50.8 (46.8 to 51.8)	26.6 (7.8 to 41.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Physical Summary Score (PhS) at 48 weeks

End point title	CHQ Physical Summary Score (PhS) at 48 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

48 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	2		
Units: Units				
median (inter-quartile range (Q1-Q3))	54.3 (52.4 to 55.9)	16.8 (12.8 to 20.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Physical Summary Score (PhS) at 72 weeks

End point title	CHQ Physical Summary Score (PhS) at 72 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	48.7 (48.2 to 55.4)	38.7 (18.3 to 51.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Psychosocial Summary Score (PsS) at Baseline

End point title	CHQ Psychosocial Summary Score (PsS) at Baseline

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

Baseline

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: unit(s)s				
median (inter-quartile range (Q1-Q3))	34.9 (32.5 to 48.1)	28.9 (25.0 to 32.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Psychosocial Summary Score (PsS) at 16 weeks

End point title	CHQ Psychosocial Summary Score (PsS) at 16 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

16 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Units				
median (inter-quartile range (Q1-Q3))	52.0 (48.4 to 60.1)	42.8 (39.9 to 43.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Psychosocial Summary Score (PsS) at 24 weeks

End point title	CHQ Psychosocial Summary Score (PsS) at 24 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

24 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	60.7 (58.2 to 65.5)	39.1 (25.7 to 52.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Psychosocial Summary Score (PsS) at 48 weeks

End point title	CHQ Psychosocial Summary Score (PsS) at 48 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

48 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	2		
Units: Units				
median (inter-quartile range (Q1-Q3))	54.3 (53.5 to 56.5)	24.8 (15.3 to 34.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: CHQ Psychosocial Summary Score (PsS) at 72 weeks

End point title	CHQ Psychosocial Summary Score (PsS) at 72 weeks

End point description:

The Child Health Questionnaire™ (CHQ) is a family of generic person-reported outcomes measures to assess health-related quality of life for children and adolescents from 5-to-18 years of age. Two sub-scores are derived: Physical Summary Score (PhS); and Psychosocial Summary Score (PsS)

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Units				
median (inter-quartile range (Q1-Q3))	59.0 (57.8 to 60.2)	52.4 (38.5 to 58.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Oral Corticosteroid dose at 24 weeks

End point title	Cumulative Oral Corticosteroid dose at 24 weeks
End point description:	
Total oral corticosteroid prescribed from randomisation to 24 weeks	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: mg/kg				
median (inter-quartile range (Q1-Q3))	51.6 (51.0 to 52.0)	50.7 (50.3 to 50.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Oral Corticosteroid dose at 72 weeks

End point title	Cumulative Oral Corticosteroid dose at 72 weeks
End point description:	
Total oral corticosteroid prescribed from randomisation to 72 weeks	
End point type	Secondary
End point timeframe:	
72 weeks	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mg/kg				
median (inter-quartile range (Q1-Q3))	74.0 (73.9 to 77.6)	73.1 (72.7 to 73.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Height z-score at 72 weeks

End point title	Height z-score at 72 weeks

End point description:

Age and sex adjusted z-scores for height. A score of 0 means average height for that age/sex. Scores below -2 and above 2 indicate very unusual heights for age/sex.

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: z-score				
median (inter-quartile range (Q1-Q3))	-1.0 (-1.1 to 1.0)	0.0 (-0.2 to 0.1)		

Attachments (see zip file)	MMF Height Z-scores: Profile plots/Fig 6-10a.png CYC Height Z-scores: Profile plots/Fig 6-10b.png

Statistical analyses

No statistical analyses for this end point

Secondary: Weight z-score at 72 weeks

End point title	Weight z-score at 72 weeks

End point description:

Age and sex adjusted z-scores for weight. A score of 0 means average weight for that age/sex. Scores below -2 and above 2 indicate very unusual weights for age/sex.

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Z-score				
median (inter-quartile range (Q1-Q3))	-0.5 (-0.5 to -0.5)	1.6 (1.0 to 2.3)		

Attachments (see zip file)	MMF Weight Z-scores: Profile plots/Fig 6-11a.png CYC Weight Z-scores: Profile plots/Fig 6-11b.png

Statistical analyses

No statistical analyses for this end point

Secondary: BMI z-score at 72 weeks

End point title	BMI z-score at 72 weeks

End point description:

Age and sex adjusted z-scores for BMIt. A score of 0 means average BMI for that age/sex. Scores below -2 and above 2 indicate very unusual BMI for age/sex.

End point type	Secondary

End point timeframe:

72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: z-score				
median (inter-quartile range (Q1-Q3))	-0.3 (-0.4 to 0.0)	1.5 (1.3 to 2.4)		

Attachments (see zip file)	MMF BMI Z-scores: Profile plots/Fig 6-12a.png CYC BMI Z-scores: Profile plots/Fig 6-12b.png

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse rate

End point title	Relapse rate

End point description:

A relapse is defined as a PVAS score > 0 occurring after remission.
In addition to the remission rate, it was also planned to report time-to-relapse, and rates of major/minor relapses. However, as no relapses were observed, we simply report the relapse rate.

End point type	Secondary

End point timeframe:

From point of remission to 72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: At least one adverse event, which may including drug toxicity

End point title	At least one adverse event, which may including drug toxicity

End point description:

End point type	Secondary

End point timeframe:

From randomisation to 72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Subjects	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time from randomisation to death

End point title	Time from randomisation to death

End point description:

The endpoint was planned as a time-to-event. However, as no subjects died, we report this as a rate.

End point type	Secondary

End point timeframe:

From randomisation to 72 weeks

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality-adjusted life years (QALYs)

End point title	Quality-adjusted life years (QALYs)

End point description:

Measure of utility of treatments

End point type	Secondary

End point timeframe:

Randomisation to 18 months

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: QALY				
arithmetic mean (confidence interval 95%)	1.13 (0.58 to 1.44)	1.18 (1.07 to 1.48)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)

Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.047
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.575
upper limit	0.48

Secondary: Probability of cost-effectiveness at £20,000 per QALY threshold

End point title	Probability of cost-effectiveness at £20,000 per QALY threshold
End point description:	
Cost-effectiveness acceptability	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Probability				
number (not applicable)	0.32	0.68		

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of cost-effectiveness at £30,000 per QALY threshold

End point title	Probability of cost-effectiveness at £30,000 per QALY threshold
End point description:	
Probability of cost-effectiveness at £30,000 per QALY threshold	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Probability				
number (not applicable)	0.34	0.66		

Statistical analyses

No statistical analyses for this end point

Secondary: Disaggregated 18-month costs: Day-case admittance

End point title	Disaggregated 18-month costs: Day-case admittance
End point description:	
Total costs associated with admission to hospital where an overnight stay was not required	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	4261 (-2842 to 11365)	1053 (-612 to 2718)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	3208
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1786
upper limit	12112

Secondary: Disaggregated 18-month costs: Out-patient clinic	
End point title	Disaggregated 18-month costs: Out-patient clinic
End point description: Costs associated with out-patient clinic attendance	
End point type	Secondary
End point timeframe: Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	74 (-67 to 215)	1036 (296 to 1998)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-962
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1835
upper limit	-83

Secondary: Disagreggated 18 month costs: General ward visit	
End point title	Disagreggated 18 month costs: General ward visit
End point description: Cost arising from general ward visits	
End point type	Secondary
End point timeframe: Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	341 (-68 to 852)	272 (-99 to 644)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-486
upper limit	623

Secondary: Disagreggated 18 month costs: Concomitant medications

End point title	Disagreggated 18 month costs: Concomitant medications
End point description:	
Costs arising from concomitant medications	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	281 (108 to 505)	682 (96 to 1933)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-401
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1670
upper limit	255

Secondary: Disagreggated 18 month costs: Azathioprine	
End point title	Disagreggated 18 month costs: Azathioprine
End point description: Costs associated with the medication Azathioprine	
End point type	Secondary
End point timeframe: Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	30 (21 to 41)	1542 (27 to 6047)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)

Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-1512
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6015
upper limit	3

Secondary: Disagreggated 18 month costs: Cyclophosphamide

End point title	Disagreggated 18 month costs: Cyclophosphamide
End point description:	
Costs associated with the treatment Cyclophosphamide (CYC treatment arm only)	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Intravenous Cyclophosphamide (CYC)			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	380 (297 to 468)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disagreggated 18 month costs: Mycophenolate mofetil

End point title	Disagreggated 18 month costs: Mycophenolate mofetil
End point description:	
Costs associated with the treatment Mycophenolate mofetil (MMF treatment arm only)	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	976 (98 to 3204)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disagreggated 18 month costs: Corticosteroids

End point title	Disagreggated 18 month costs: Corticosteroids
End point description: Costs associated with corticosteroids	
End point type	Secondary
End point timeframe: Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	52 (42 to 60)	57 (41 to 67)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	12

Secondary: Mean total discounted costs

End point title	Mean total discounted costs
End point description:	
Total costs associated with each treatment group	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP(£)				
arithmetic mean (confidence interval 95%)	6071 (640 to 15555)	4725 (1480 to 7157)		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	1346
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4709
upper limit	11175

Secondary: Incremental net health benefit (INHB): Cost effectiveness threshold £20,000 per QALY

End point title	Incremental net health benefit (INHB): Cost effectiveness threshold £20,000 per QALY
End point description:	
End point type	Secondary
End point timeframe:	
Randomisation to 18 months	

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP per QALY				
arithmetic mean (confidence interval 95%)	0.826 (0.327 to 1.297)	0.944 (0.465 to 1.406)		

Statistical analyses

Statistical analysis title	Incremental analysis
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Mean difference (final values)
Point estimate	-0.114
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.574

Notes:

[4] - Incremental analysis

Secondary: Incremental net health benefit (INHB): Cost effectiveness threshold £30,000 per QALY

End point title	Incremental net health benefit (INHB): Cost effectiveness threshold £30,000 per QALY

End point description:

End point type	Secondary

End point timeframe:

Randomisation to 18 months

End point values	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: GBP per QALY				
arithmetic mean (confidence interval 95%)	0.931 (0.482 to 1.363)	1.020 (0.622 to 1.414)		

Statistical analyses

Statistical analysis title	Incremental analysis
Comparison groups	Mycophenolate mofetil (MMF) v Intravenous Cyclophosphamide (CYC)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Mean difference (final values)
Point estimate	-0.092
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.695
upper limit	0.5

Notes:

[5] - Incremental analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Randomisation to 72 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	Mycophenolate mofetil (MMF)
Reporting group description: -	
Reporting group title	Intravenous Cyclophosphamide (CYC)
Reporting group description: -	

Serious adverse events	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	0 / 5 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Mycophenolate mofetil (MMF)	Intravenous Cyclophosphamide (CYC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	5 / 5 (100.00%)	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Mood altered			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Investigations			

White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	7	
Blood iron decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Laboratory test abnormal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Red blood cell sedimentation rate increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Avulsion fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Back injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	

Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	3	
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Mouth ulceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Supernumerary teeth			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin striae			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 6 (50.00%)	2 / 5 (40.00%)	
occurrences (all)	4	2	
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Gastroenteritis viral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Helicobacter infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Lower respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2014	Changes to Protocol. Documents submitted: Protocol V2.0. Protocol section 10.2.3 amended so that the reference to 48 weeks as been deleted as advised. Protocol section 5.2, exclusion criteria revised to state that sexually active females are excluded if they are not prepared to use two reliable means of contraception for the complete duration of the trial and for 12 months after study drug therapy is discontinued. Protocol section 7.10.1 amended to state that "For patients of reproductive potential (males and females), use of reliable means of contraception as stated in Exclusion Criteria is required throughout study participation and for 12 months after study drug therapy is discontinued." Abstinence is acceptable in the trial and section 5.2, exclusion criteria 15 has been amended to show abstinence is acceptable only if it is the preferred and usual lifestyle of the patient. Protocol section 7.3.2 has been updated to state that protection from UV-light exposure is mandatory and patients should wear sunscreen SPF 50+ when exposed to UV-light. Protocol section 2.4 has also been updated to add UV-light exposure as a potential trial risk. Protocol section 7.10.2 has been updated to state that live vaccinations are not permitted for the duration of the trial period. The protocol has been updated following the telephone conversation with Farhat Gilani Pharmacovigilance Manager, University College London, to show that SAE's which are not related to disease progression will be reported within 24 hours of becoming aware of the event. SAE's that are symptoms due to disease progression will be reported on the adverse event forms which are submitted within fourteen days of the patient visit. A MYPAN website will be created at the address www.mypantrial.org.uk. The website will display information about the trial, including a summary, location of the sites involved, links to collaborators, methods of contacting the trial team and updates on recruitment figures.
26 October 2015	Addition of UK site – Addenbrookes Hospital Removal of UK Site – Queens Medical Centre, Nottingham
17 December 2015	Changes to Protocol. Documents submitted: Protocol V3.0, Amendment assessment form, Notification of substantial amendment, Cover letter, SmPC Cellcept oral suspension, SmPC Cellcept 250mg, SmPC Cellcept 500mg
29 February 2016	Addition of two UK sites: University College London University Hospital and Royal Free Hospital Removal of UK Site – Bristol University Hospital
04 May 2016	Substantial changes have been made to the contraceptive advice in the SmPC for Mycophenolate Mofetil. This advice is now reflected in the updated PISCs for the adults and parents.
26 October 2016	The IRAS form has been updated to declare the use of X-Rays as a screening tool to rule out infections prior to commencement in the study. The patient information sheets and consent forms have been updated to give participants more information about the use of X-Rays as part of the study and the risks involved.

17 July 2017	Documents submitted: Protocol V4.0. Recruitment period extended from 30th January 2018 to 0th June 2018 Section 5.1: Inclusion criteria. Text updated to clarify that if the patient was not adequately treated at the time of diagnosis then they may still be eligible for the study. Section 9: Removal of interim monitoring and analysis Section 10.9.2: Clarification of urgent safety measures reporting procedures
24 May 2018	GDPR information letter sent out to patient and parents, including information correctly notifying them about the way their consent forms have been handled. Section 4.4. and 4.8 amended with new RSI information
28 November 2019	Update to the Reference Safety Information (section 4.4 and 4.8) for the trial after an update to the SmPC for Cellcept.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported