

**Clinical trial results:****A pilot study on the effects of an alternate-day corticosteroid regimen in children with active crohn's disease****Summary**

EudraCT number	2010-022017-26
Trial protocol	GB
Global end of trial date	11 March 2014

Results information

Result version number	v1 (current)
This version publication date	29 March 2020
First version publication date	29 March 2020

Trial information**Trial identification**

Sponsor protocol code	R01116
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	REC reference: 10/H1010/53

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	Oxford Road, Manchester, United Kingdom, M13 9WL
Public contact	Dr Lynne Webster, Manchester University NHS Foundation Trust, research.sponsor@mft.nhs.uk
Scientific contact	Dr Lynne Webster, Manchester University NHS Foundation Trust, research.sponsor@mft.nhs.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	11 March 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 March 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the feasibility of a RCT to compare an alternate-day prednisolone regimen with a daily-dose regimen:

- a. to assess whether the research protocol is realistic and workable
- b. to identify logistical problems which might occur using the proposed protocol
- c. to assess the likely success of recruitment and determine period of recruitment
- d. to determine if there is likely to be significant attrition
- e. to determine what resources (finance, staff) will be needed for the main study
- f. to test the outcome measures and their suitability, practicality, statistical properties and utility.

Protection of trial subjects:

The potential risks of this study include adverse reactions to prednisolone and the small risk of venepuncture. However, the potential benefits of this study far outweigh the potential risks. We do not expect the occurrence of prednisolone adverse effects to be any worse than what is seen in routine clinical practice. Patients who are randomised to alternateday therapy may however experience fewer side effects although it is likely that alternateday therapy may be less effective. We will closely monitor all participants for any evidence of adverse effects and also of disease activity over the study period. Venepuncture will be undertaken by experienced nurses or doctors and where appropriate, a local analgesia will be applied in order to minimise the pain and discomfort associated with bloodtaking.

Participants and/or their parents/carers will have to spend some time to complete the quality of life questionnaire but this questionnaire is quite simple and each should not take more than 10 minutes to complete.

Apart from being assigned to either alternateday therapy or dailydose therapy, patients in both groups will be treated in exactly the same way.

Background therapy:

Routine care in both groups will remain as it is in normal practice.

Evidence for comparator:

N/A - no comparator used.

Actual start date of recruitment	31 August 2011
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: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	6
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients who satisfied entry criteria were approached by an investigator who provided full information about the study and obtain written informed consent. By means of computer-generated random number, participants were randomly allocated to one of two groups: Group 1 (alternateday corticosteroid regimen) or Group 2 (dailydose corticosteroid regim

Pre-assignment

Screening details:

Inclusion:

- 1) patients aged 8 to 17 years
- 2) diagnosis of Crohn's disease by established clinical, endoscopic, histological and radiological criteria
- 3) clinically active disease defined as a paediatric Crohn's disease activity index (PCDAI) score of >15
- 4) clinical decision made to commence oral prednisolone
- 5) parental and child consent

Pre-assignment period milestones

Number of subjects started	7
Number of subjects completed	7

Period 1

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

Blinding implementation details:

N/A - this was an open label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (alternate-day corticosteroid regimen)

Arm description:

Group 1 (alternate-day corticosteroid regimen): oral prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then switch to alternate-day dosing and reduce dose by 5mg after every week.

Arm type	Experimental
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	A07EA01
Other name	PL 06464/0914
Pharmaceutical forms	Soluble tablet
Routes of administration	Oral use

Dosage and administration details:

Oral prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks

Arm title	Group 2 (daily-dose corticosteroid regimen)
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Arm description:

Group 2 (daily-dose corticosteroid regimen): oral Prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then reduce dose by 5 mg every week as daily dose. Participants will take each daily dose in the morning.

Arm type	Active comparator
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Investigational medicinal product name	Prednisolone
Investigational medicinal product code	A07EA01
Other name	PL 06464/0914
Pharmaceutical forms	Soluble tablet
Routes of administration	Oral use

Dosage and administration details:

Oral Prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then reduce dose by 5 mg every week as daily dose.

Number of subjects in period 1	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily-dose corticosteroid regimen)
Started	5	2
Completed	0	0
Not completed	5	2
Consent withdrawn by subject	3	-
Trial withdrawn	2	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	Group 1 (alternate-day corticosteroid regimen)
Reporting group description: Group 1 (alternate-day corticosteroid regimen): oral prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then switch to alternate-day dosing and reduce dose by 5mg after every week.	
Reporting group title	Group 2 (daily-dose corticosteroid regimen)
Reporting group description: Group 2 (daily-dose corticosteroid regimen): oral Prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then reduce dose by 5 mg every week as daily dose. Participants will take each daily dose in the morning.	

Primary: Clinical remission defined as a Paediatric Crohn's Disease Activity Index (PCDAI) score of < 10

End point title	Clinical remission defined as a Paediatric Crohn's Disease Activity Index (PCDAI) score of < 10 ^[1]
End point description:	
End point type	Primary
End point timeframe: The PCDAI will be assessed at baseline or screening, 3, 6, and 11 weeks.	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Data analysis was not conducted as the trial was terminated early.	

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily-dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: 99999				
number (not applicable)				

Notes:

[2] - The trial was terminated early so no results were analysed.

[3] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Health related quality of life

End point title	Health related quality of life
End point description:	
End point type	Secondary
End point timeframe: QOL scores will be assessed at baseline, six and 11 weeks.	

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: 99999				

Notes:

[4] - The trial was terminated early so no results were analysed.

[5] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response – defined as a 15 point drop of PCDAI from baseline

End point title	Clinical response – defined as a 15 point drop of PCDAI from baseline
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End point description:

End point type	Secondary
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End point timeframe:

Clinical response will be defined as a 15 point drop of PCDAI from baseline values.

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: 99999				

Notes:

[6] - The trial was terminated early so no results were analysed.

[7] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of prednisolone therapy on bone formation and bone resorption

End point title	Effect of prednisolone therapy on bone formation and bone resorption
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End point description:

End point type	Secondary
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End point timeframe:

Samples will be analysed at baseline, 6 weeks, and 11 weeks for biochemical markers of bone formation.

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	0 ^[9]		
Units: 99999				

Notes:

[8] - The trial was terminated early so no results were analysed.

[9] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of Prednisolone therapy on Insulin-like Growth Factor 1

End point title	Effect of Prednisolone therapy on Insulin-like Growth Factor 1
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End point description:

End point type	Secondary
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End point timeframe:

Serum IGF-1 will be assessed at baseline and at 11 weeks.

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[10]	0 ^[11]		
Units: 99999				

Notes:

[10] - The trial was terminated early so no results were analysed.

[11] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Adrenal responsiveness to ACH measured using a standard synacthen test protocol

End point title	Adrenal responsiveness to ACH measured using a standard synacthen test protocol
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End point description:

End point type	Secondary
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End point timeframe:

Adrenal responsiveness to Adrenocorticotrophic Hormone (ACTH) will be measured using a standard synacthen test protocol

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[12]	0 ^[13]		
Units: 99999				

Notes:

[12] - The trial was terminated early so no results were analysed.

[13] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse effects

End point title	Adverse effects
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End point description:

End point type	Secondary
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End point timeframe:

At each scheduled visit (3, 6, and 11 weeks), the investigator will ask each participant to report any event(s) that the participant, or the parents, believe might reasonably be related to participation in this study.

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[14]	0 ^[15]		
Units: 99999				

Notes:

[14] - The trial was terminated early so no results were analysed.

[15] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Adherence to Prednisolone Therapy

End point title	Adherence to Prednisolone Therapy
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End point description:

End point type	Secondary
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End point timeframe:

Using pill counts conducted at 3, 6, and 11 weeks.

End point values	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily- dose corticosteroid regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[16]	0 ^[17]		
Units: 99999				

Notes:

[16] - The trial was terminated early so no results were analysed.

[17] - The trial was terminated early so no results were analysed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

An adverse event is the appearance or worsening of any undesirable sign, symptom, or medical condition occurring after the study has commenced, even if not considered to be related to the investigational medicinal product.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Group 1 (alternate-day corticosteroid regimen)
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Reporting group description:

Group 1 (alternate-day corticosteroid regimen): oral prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then switch to alternate-day dosing and reduce dose by 5mg after every week.

Reporting group title	Group 2 (daily-dose corticosteroid regimen)
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Reporting group description:

Group 2 (daily-dose corticosteroid regimen): oral Prednisolone 2 mg/kg/day (max 40 mg) for 3 weeks, then reduce dose by 5 mg every week as daily dose. Participants will take each daily dose in the morning.

Serious adverse events	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily-dose corticosteroid regimen)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Presentation to A&E for increased abdo pain and increased inflammatory markers			
subjects affected / exposed ^[1]	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Three participants withdrew before treatment was administered.

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

Non-serious adverse events	Group 1 (alternate-day corticosteroid regimen)	Group 2 (daily-dose corticosteroid regimen)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	2 / 2 (100.00%)	

Blood and lymphatic system disorders Increased blood glucose. subjects affected / exposed ^[2] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Iron deficiency subjects affected / exposed ^[3] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
General disorders and administration site conditions Headache during Synachen administration subjects affected / exposed ^[4] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Sub optimal response to Synachen subjects affected / exposed ^[5] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Ankle pain/shin pain subjects affected / exposed ^[6] occurrences (all)	0 / 2 (0.00%) 0	1 / 2 (50.00%) 1	
Headache subjects affected / exposed ^[7] occurrences (all)	0 / 2 (0.00%) 0	1 / 2 (50.00%) 1	
Gastrointestinal disorders Abdominal cramps subjects affected / exposed ^[8] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Loose stools and increased frequency subjects affected / exposed ^[9] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Mild epigastric discomfort subjects affected / exposed ^[10] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Blood in stools subjects affected / exposed ^[11] occurrences (all)	0 / 2 (0.00%) 0	1 / 2 (50.00%) 1	
Increase in stools and abdominal pain			

subjects affected / exposed ^[12] occurrences (all)	0 / 2 (0.00%) 0	1 / 2 (50.00%) 1	
Respiratory, thoracic and mediastinal disorders Cough and cold subjects affected / exposed ^[13] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Chest pain, tightening subjects affected / exposed ^[14] occurrences (all)	0 / 2 (0.00%) 0	1 / 2 (50.00%) 1	
Skin and subcutaneous tissue disorders Rounder face/cheeks subjects affected / exposed ^[15] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	
Musculoskeletal and connective tissue disorders Increase in joint pain subjects affected / exposed ^[16] occurrences (all)	1 / 2 (50.00%) 1	0 / 2 (0.00%) 0	

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Three participants withdrew before treatment was administered.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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Justification: Three participants withdrew before treatment was administered.

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Justification: Three participants withdrew before treatment was administered.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2012	Due to local changes regarding blood sample collection and analysis it has become necessary to amend the protocol. In order to avoid amendments to the protocol every time the method of sample collection or analysis is amended, it has been decided to remove the laboratory section (sample collection, storage and analysis) to a separate laboratory manual. This will be version controlled by the research team and amended as required.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Only 4 of a planned 27 patients completed treatment which is insufficient to allow a complete evaluation of the results and complete the overall risk benefit assessment of the IMP.
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Notes: