Clinical trial results:
The effect of prednisolone versus hydrocortisone as glucocorticoid replacement therapy on hypoglycaemia frequency in people with Type 1 diabetes and adrenal insufficiency: a pilot study.

Summary

EudraCT number	2008-002336-15
Trial protocol	GB
Global end of trial date	20 September 2017

Results information

Result version number	v1 (current)
This version publication date	03 May 2019
First version publication date	03 May 2019
Summary attachment (see zip file)	FINAL STUDY REPORT (Reason for lack of results for prednisolone trial.pdf)

Trial information

Trial identification

Sponsor protocol code	578

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Prof Stephanie Amiel, King's College London, +44 0207848 5639, stephanie.amiel@kcl.ac.uk
Scientific contact	Prof Stephanie Amiel, King's College London, +44 0207848 5639, stephanie.amiel@kcl.ac.uk
Sponsor organisation name	King's College Hospital
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE59RS
Public contact	Prof Stephanie Amiel, King's College London, +44 0207848 5639, stephanie.amiel@kcl.a.uk
Scientific contact	Prof Stephanie Amiel, King's College London, +44 0207848 5639, stephanie.amiel@kcl.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	20 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 September 2017
Global end of trial reached?	Yes
Global end of trial date	20 September 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

In people with type 1 diabetes and adrenal insufficiency, who are established on hydrocortisone as glucocorticoid replacement, frequency of nocturnal hypoglycaemia will be reduced by changing the glucocorticoid replacement from hydrocortisone to prednisolone

Protection of trial subjects:

The trial included a familiarisation phase: 1 week The purpose of this phase is to familiarise study participants with the monitoring and recording processes required for the study and provide some baseline data. Participants to take their normal hydrocortisone regimen, as prescribed by their doctor. Insulin self adjustment and recording: o Participants to continue their normal insulin regimen. Dose adjustment according to their usual principles of flexible insulin therapy encouraged. o Participants to record their insulin doses taken in the DAFNE (Dose Adjustment For Normal Eating) Diary provided Self blood glucose monitoring: o Participants to continue usual monitoring of capillary blood glucose levels with a minimum of four readings per day. To record all capillary blood glucose readings taken in the DAFNE Diary provided o Participants to check capillary blood glucose readings at 3 am on one occasion during the week. Hypoglycaemia reporting: Participants to record details of all hypoglycaemic events on the Hypoglycaemia Record Sheet provided. To report all levels < 3mmol/l and provide details of the episode including time, glucose level, symptoms, recognition, treatment and possible precipitant. Adverse event / missed medication recording: participants to record unusual events (eg exercise/illness) and missed medication in the DAFNE Diary

Background therapy:

The study lasts eleven weeks for each participant and consists of a one week familiarisation phase followed by the five week prednisolone phase and the five week hydrocortisone phase in random order. The study includes eight hospital visits. Extra visits may be required if the CGMS sensor stops working and needs to be replaced

Evidence for comparator: -

Actual start date of recruitment	20 December 2012
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: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the diabetes department of King's College Hospital NHS Foundation Trust. The first patient was recruited in December 2012. Only 2 further patients were recruited and the trial was terminated early in September 2017 due to lack of recruitment.

Pre-assignment

Screening details:

1. Age 2. Sex 3. Weight and height 4. Ethnic group 5. Date of diagnosis of diabetes 6. Current insulin regimen and start date 7. Date of participation in a DAFNE (Dose Adjustment For Normal Eating) course or similar 8. Presence of diabetes microvascular complications .

Period 1

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

Blinding implementation details:

This was an open label study.
Participants will be randomised to either:
hydrocortisone phase followed by prednisolone phase,
or prednisolone phase followed by hydrocortisone phase.

Arms

Arm title	Whole trial

Arm description:

Participants will be randomised to either: hydrocortisone phase followed by prednisolone phase, prednisolone phase followed by hydrocortisone phase.

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

Dosage and administration details:

15mg - prednisolone will be calculated equivalent to normal hydrocortisone regimen. Normal daily dose of hydrocortisone will be converted into the equivalent total dose of prednisolone using hydrocortisone 20mg = prednisolone 5mg.
Up to 15 mg per day in total

Investigational medicinal product name	Hydrocortisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Maximum dose allowed 30 mg

Number of subjects in period 1	Whole trial
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Whole trial period

Reporting group description: -

Reporting group values	Whole trial period	Total	
Number of subjects	3	3	
Age categorical			
Only adult patients recruited			
Units: Subjects			
Adults (18-64 years)	3	3	
Gender categorical Units: Subjects			
Female	2	2	
Male	1	1	

End points

End points reporting groups

Reporting group title	Whole trial

Reporting group description:

Participants will be randomised to either: hydrocortisone phase followed by prednisolone phase, prednisolone phase followed by hydrocortisone phase.

Primary: Frequency of moderate nocturnal biochemical hypoglycaemia

End point title	Frequency of moderate nocturnal biochemical hypoglycaemia[1]

End point description:

End point type	Primary

End point timeframe:

From randomisation to last dose of IMP.

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: No statistical analysis was possible for this trial as the trial terminated early due to lack of recruitment

End point values	Whole trial			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: episodes of low interstitial glucose	0			

Attachments (see zip file)	Lack of data for analysis/Reason for lack of results for

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: From consent to final study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Whole trial
Reporting group description: -	

Serious adverse events	Whole trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Whole trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		

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: Hperglycaemia and hypoglycaemia were non-reportable AEs for this trial. No other AEs were reported for the 3 patients who completed treatment.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported