Clinical trial results:
Do sulphponylureas preserve cortical function during hypoglycaemia in patients with type 1 diabetes and hypoglycaemia unawareness?

Summary

EudraCT number	2007-000497-23
Trial protocol	GB
Global end of trial date	22 February 2014

Results information

Result version number	v1 (current)
This version publication date	26 April 2019
First version publication date	26 April 2019

Trial information

Trial identification

Sponsor protocol code	07/Q0703/18

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College Hospital
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE59RS
Public contact	Dr Pratik Choudhary , King's College Hospital, +44 203 299 9000, pratik.choudhary@kcl.ac.uk
Scientific contact	Dr Pratik Choudhary , King's College Hospital, +44 0203 299 9000, pratik.choudhary@kcl.ac.uk
Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Dr Pratik Choudhary , King's College London, +44 203 299 9000, pratik.choudhary@kcl.ac.uk
Scientific contact	Dr Pratik Choudhary , King's College London, +44 203 299 9000, pratik.choudhary@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	22 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2014
Global end of trial reached?	Yes
Global end of trial date	22 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To see if the use of sulphonylureas (glibenclamide) can help preserve symptoms or cognitive function during hypoglycaemia
Specifically to see if the use of sulphonylureas can -
1. Increase the symptoms in response to low blood glucose levels
2. Improve performance in brain function tests during low blood glucose levels
3. Increase the protective hormone responses to low blood glucose levels

Protection of trial subjects:

At screening subjects will undergo physical examination and screening blood tests (liver and renal function).
Any side effects reported will be documented according to trust policy and GCP guidelines including start, duration, severity and outcome.

Background therapy:

Patients continued on their usual background therapy

Evidence for comparator: -

Actual start date of recruitment	23 April 2008
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from one clinical site between 2008 and 2014

Pre-assignment

Screening details:

• Age 18-75
• Type 1 diabetes (WHO definition) of at least 5 years duration
• History of impaired awareness of hypoglycaemia (capillary glucose readings <3.5mmol/l without symptoms on > 3 occasions in the past 3 months (those with
intact symptoms will be unlikely to show an improvement and would not really
benefit from taking any medication i

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Participants will

Arms

Arm title	Full study

Arm description:

Each subject will undergo 2 studies in random order, separated by not less than 2 weeks, having taken 7 days of either placebo or glibenclamide (a sulphonylurea). In each study, we will lower the blood sugar level gradually through a number of steps in a safe and controlled manner. At each step we will measure symptoms of low blood glucose and also ask the patient to perform a battery of computer based cognitive function tests designed to look at certain aspects of brain function.

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

Dosage and administration details:

Each subject will undergo 2 studies in random order, separated by not less than 2 weeks, having taken 7 days of either placebo or 10mg glibenclamide

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

Dosage and administration details:

Each subject will undergo 2 studies in random order, separated by not less than 2 weeks, having taken 7 days of either placebo or 10mg glibenclamide

Number of subjects in period 1	Full study
Started	15
Completed	10
Not completed	5
Physician decision	1
Cannula failures	3
Pregnancy	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Full study

Reporting group description:

Each subject will undergo 2 studies in random order, separated by not less than 2 weeks, having taken 7 days of either placebo or glibenclamide (a sulphonylurea). In each study, we will lower the blood sugar level gradually through a number of steps in a safe and controlled manner. At each step we will measure symptoms of low blood glucose and also ask the patient to perform a battery of computer based cognitive function tests designed to look at certain aspects of brain function.

Primary: Preservation of cortical function during hypoglycaemia

End point title	Preservation of cortical function during hypoglycaemia[1]

End point description:

To obtain preliminary data to investigate if the use of sulphonylureas can help preserve symptoms or cognitive function during hypoglycaemia

End point type	Primary

End point timeframe:

During study day only.

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: Please see attached document for results.

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: whole	10			

Attachments (see zip file)	RESULTS/SULPHONUREAS.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary endpoints

End point title	Secondary endpoints

End point description:

To obtain preliminary data to see if the use of sulphonylureas can -
1. Increase the symptoms in response to low blood sugar levels
2. Improve performance in brain function tests during hypoglycaemia
3. Increase the protective hormone responses to hypoglycaemia

End point type	Secondary

End point timeframe:

During study days 1 & 2

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: whole	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Duration of the trial.

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	2 / 15 (13.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Whole Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Malignant melanoma subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 0		
General disorders and administration site conditions Lack of venous access/cannula failure subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2009	This amendment is to update the sponsorship status from single sponsorship by King's College Hospital NHS Foundation Trust to Co-sponsorship by King's College Hospital NHS Foundation Trust and King's College London. The Pharmacovigilance section has now been updated to reflect current policy and the general format has been updated into a more GCP compliant format. A few additional sections have been added for clarification but not changing the conduct of the trial. It has also been stated that subject withdrawals shall be replaced so that the 10 patients required shall complete the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported