Clinical trial results:
A Feasibility study looking at the use of Glibenclamide and metfoRmin versus stAndard Care in gEstational diabeteS

Summary

EudraCT number	2013-004706-25
Trial protocol	GB
Global end of trial date	01 November 2015

Results information

Result version number	v1 (current)
This version publication date	04 July 2020
First version publication date	04 July 2020
Summary attachment (see zip file)	Publication (s12884-017-1505-3.pdf)

Trial information

Trial identification

Sponsor protocol code	V1290413

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02080377
WHO universal trial number (UTN)	-
Other trial identifiers	ETHICS: 13/SS/0223 , CSO Funder: CZH/4/10

Notes:

Sponsors

Sponsor organisation name	University of Edinburgh
Sponsor organisation address	47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
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Sponsor organisation name	NHS Lothian
Sponsor organisation address	47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
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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	30 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 October 2015
Global end of trial reached?	Yes
Global end of trial date	01 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this feasibility study is to determine recruitment rates to a randomised trial of glibenclamide compared with insulin (both in addition to maximum tolerated metformin) for the treatment of gestational diabetes. Additionally, we will compare glycaemic control in the two groups, and evaluate acceptability. Finally, we will collect information on a range of clinical and biochemical outcomes to inform the design of a large definitive randomised trial.

Primary outcome: The number of women who agree to be randomised.

Protection of trial subjects:

The trial steering committee will monitor participants' glucose readings, paying particular attention to number and frequency of episodes of hypoglycaemia. If it is deemed that there are too many incidences of hypoglycaemia in the intervention arm then the intervention could be withdrawn and the trial stopped prematurely.

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	United Kingdom: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	23
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were given verbal and written information about the study at the time of diagnosis of GDM. Prior to
recruitment, treatment with metformin was commenced if women were failing to achieve adequate glycaemic control with lifestyle measures alone, according to standard practice.

Pre-assignment

Screening details:

All women with GDM attending the selected sites who fail monotherapy and do not meet any of the exclusion criteria will be considered to be eligible

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Glibenclamide

Arm description:

The primary aim of this feasibility study is to determine recruitment rates to a randomised trial of glibenclamide compared with insulin (both in addition to maximum tolerated metformin) for the treatment of gestational diabetes mellitus. Secondary aims will be to compare glycaemic control in the two groups, evaluate acceptability and to collect information on a range of clinical outcomes to inform the design of a large definitive randomised trial.

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

Dosage and administration details:

glibenclamide in either a 2.5 mg or 5 mg tablet. The usual dosage of glyburide is 2.5–20 mg daily in divided doses, although pharmacokinetic studies during pregnancy indicate daily doses up to 30 mg may be necessary to achieve adequate control” [15,16]. Of note, none of the six referees of the grant application related to this protocol have commented adversely on the dose of glibenclamide (reports available on request).
The dose will alter according to the clinician’s recommendations, following a strict dosing algorithm drawn up prior to the study commencing

Arm title	Insulin

Arm description: -

Arm type	Standard Care
Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

AS required

Number of subjects in period 1	Glibenclamide	Insulin
Started	13	10
Completed	13	10

Baseline characteristics

Reporting groups

Reporting group title	Glibenclamide

Reporting group description:

The primary aim of this feasibility study is to determine recruitment rates to a randomised trial of glibenclamide compared with insulin (both in addition to maximum tolerated metformin) for the treatment of gestational diabetes mellitus. Secondary aims will be to compare glycaemic control in the two groups, evaluate acceptability and to collect information on a range of clinical outcomes to inform the design of a large definitive randomised trial.

Reporting group title	Insulin

Reporting group description: -

Reporting group values	Glibenclamide	Insulin	Total
Number of subjects	13	10	23
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	33.0	34.5	
standard deviation	± 5.1	± 4.9	-
Gender categorical Units: Subjects			
Female	13	10	23
Male	0	0	0

End points

End points reporting groups

Reporting group title	Glibenclamide

Reporting group description:

The primary aim of this feasibility study is to determine recruitment rates to a randomised trial of glibenclamide compared with insulin (both in addition to maximum tolerated metformin) for the treatment of gestational diabetes mellitus. Secondary aims will be to compare glycaemic control in the two groups, evaluate acceptability and to collect information on a range of clinical outcomes to inform the design of a large definitive randomised trial.

Reporting group title	Insulin

Reporting group description: -

Primary: Number of women Randomised

End point title	Number of women Randomised

End point description:

The primary endpoint is the number (and corresponding throughput) of women who agree to be randomised

End point type	Primary

End point timeframe:

Randomisation

End point values	Glibenclamide	Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	10		
Units: not applicable	13	10		

Statistical analyses

Statistical analysis title	Number of women agreed to randomisation
Comparison groups	Glibenclamide v Insulin
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	Poisson distribution

Notes:

[1] - Feasability

[2] - As this was a feasibility study a formal power calculation was not considered appropriate

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All AEs and SAEs will be recorded from the time a participant signs the consent form to take part in the study until stopping the IMP or discharge following delivery of the baby, whichever is later

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	0

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

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: All adverse medical events reported by the participant were noted in the participant's hospital notes, together with a note of the date of starting, the duration, and any medical treatment received. The clinician will assess ALL reported AEs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 April 2014	Increased detail, changes to flow chart, change in secondary outcomes, NIMP and Imp supply, clarification on rand process, stats analysis and TSC/DMC details
17 December 2014	Lower limit of gestation (weeks) from 20+0 weeks gestation to 16+0 weeks gestation. It also includes some minor clarifications in the protocol, consent form and PIL, as well as the opening of recruitment in another hospital

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.

The limitations of the study include the small sample size, which could have contributed to a chance imbalance on prognostic factors including weight and time of diagnosis.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28938877