Clinical trial results:
Prevention of metabolic complications of glucocorticoid excess

Summary

EudraCT number	2008-005708-18
Trial protocol	GB
Global end of trial date	24 April 2017

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019
Summary attachment (see zip file)	Adverse event deatils (SAEs_METGC.xlsx)

Trial information

Trial identification

Sponsor protocol code	14081962

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01319994
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Queen Mary University
Sponsor organisation address	5 Walden St, London, United Kingdom, E1 2EF
Public contact	Marie-Claire Rickard, Queen Mary University, m.rickard@qmul.ac.uk
Scientific contact	Marie-Claire Rickard, Queen Mary University, m.rickard@qmul.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 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2017
Global end of trial reached?	Yes
Global end of trial date	24 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This proposal aims to prevent or treat the deleterious metabolic consequences of glucocorticoids in patients with glucocorticoid excess

Protection of trial subjects:

Adverse events reporting and monitoring as per the agreed protocol, our sponsor, and the trial steering committee.

Background therapy:

Patients received glucocorticoid treatment as per the treating physicians.

Evidence for comparator:

Comparing the effect of Metformin 850mg TDS to placebo.

Actual start date of recruitment	12 July 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: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	52
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects initiated on glucocorticoid treatment at the same time as the trial treatment were recruited into the "Prevention algorithm". Subjects already on established glucocorticoids were recruited into the "Treatment algorithm". The recruitment into the "Prevention algorithm" ended up not feasible and not analysed.

Pre-assignment

Screening details:

patients on glucocorticoid treatment

Pre-assignment period milestones

Number of subjects started	53[1]
Number of subjects completed	53

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: this inconsistency is due to withdraws prior to commencing treatment

Period 1

Period 1 title	Overall trial ("Treatment algorithm") (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention ("Treatment algorithm")

Arm description:

Metformin 850mg TDS

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

Dosage and administration details:

Period of titration aiming for 850mg TDS

Arm title	Placebo ("Treatment algorithm")

Arm description:

Patients on established glucocorticoids who received placebo during the study.

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

Dosage and administration details:

Tablets 850mg TDS (titrated as per protocol)

Number of subjects in period 1[2]	Intervention ("Treatment algorithm")	Placebo ("Treatment algorithm")
Started	26	27
Completed	19	21
Not completed	7	6
Protocol deviation	7	6

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: this inconsistency is due to withdraws prior to commencing treatment

Baseline characteristics

Reporting groups	
Reporting group title	Intervention ("Treatment algorithm")
Reporting group description:	
Metformin 850mg TDS	
Reporting group title	Placebo ("Treatment algorithm")
Reporting group description:	
Patients on established glucocorticoids who received placebo during the study.	

Reporting group values	Intervention ("Treatment algorithm")	Placebo ("Treatment algorithm")	Total
Number of subjects	26	27	53
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	47	45	
standard deviation	± 15	± 15	-
Gender categorical			
Units: Subjects			
Female	14	15	29
Male	12	12	24

End points

End points reporting groups

Reporting group title	Intervention ("Treatment algorithm")
Reporting group description: Metformin 850mg TDS	
Reporting group title	Placebo ("Treatment algorithm")
Reporting group description: Patients on established glucocorticoids who received placebo during the study.	
Subject analysis set title	change in the visceral to subcutaneous fat area ratio
Subject analysis set type	Intention-to-treat
Subject analysis set description: Comparing the change in the interventional vs placebo treatment arms.	

Primary: Change in the visceral to subcutaneous fat area ratio

End point title	Change in the visceral to subcutaneous fat area ratio[1]
End point description: Assessed by a computer tomography, the primary outcome was the difference between the treatment groups in the body composition change over 12 weeks.	
End point type	Primary
End point timeframe: 12 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: No analysis supplied by CI

End point values	change in the visceral to subcutaneous fat area ratio			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: ratio				
arithmetic mean (confidence interval 95%)	0.11 (-0.02 to 0.24)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

During a subject's participation in the trial and 30 days following the end of his/her participation.

Adverse event reporting additional description:

Please see attached document for full AE and SAE listing - due to System error in accepting data.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Intervention ("Treatment algorithm")

Reporting group description:

Metformin 850mg TDS

Reporting group title	Placebo ("Treatment algorithm")

Reporting group description:

Patients on established glucocorticoids who received placebo during the study.

Serious adverse events	Intervention ("Treatment algorithm")	Placebo ("Treatment algorithm")	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 27 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Intervention ("Treatment algorithm")	Placebo ("Treatment algorithm")	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 27 (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: Please see attached document for full AE and SAE list - system unable to accept entered data.

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