Clinical trial results:
A randomised, double-blind, placebo-controlled trial of metformin in chronic obstructive pulmonary disease (COPD) exacerbations: a pilot study

Summary

EudraCT number	2010-020818-28
Trial protocol	GB
Global end of trial date	10 April 2014

Results information

Result version number	v1 (current)
This version publication date	13 November 2019
First version publication date	13 November 2019
Summary attachment (see zip file)	Thorax Article (Thorax 2016 - Metformin in COPD trial.pdf) End of Trial Report (Metformin End of Study Report draft 1.0.doc)

Trial information

Trial identification

Sponsor protocol code	10.0086

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	St Georges University of London
Sponsor organisation address	Cranmer Terrace, London, United Kingdom, SW17 0RE
Public contact	Joint Research Office, sponsor@sgul.ac.uk, Prof Emma Baker ebaker@sgul.ac.uk, 0208725501 02087255012, sponsor@sgul.ac.uk
Scientific contact	Joint Research Office, sponsor@sgul.ac.uk, Prof Emma Baker ebaker@sgul.ac.uk, 0208725501 02087255012, ebaker@sgul.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	01 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 March 2014
Global end of trial reached?	Yes
Global end of trial date	10 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The overarching research question for this body of work is to ascertain whether metformin improves recovery from COPD exacerbations.

This pilot study will address a more limited question, as a basis for future trial design: in patients admitted to hospital with COPD exacerbations, is metformin an effective treatment for acute hyperglycaemia (elevated blood sugar concentration)?

Protection of trial subjects:

This trial will be monitored on a daytoday
basis by the study team. Oversight will be provided by the steering
committee, chaired by the chief investigator. A patient representative, and a researcher from outside the trial group,
shall be invited to attend steering group meetings. No interim data analyses are planned

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 January 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: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment within UK only.

Pre-assignment

Screening details:

Baseline measurements will then be taken. This will include a validated 8item
questionnaire to quantify the impact
that COPD is having on the patients' wellbeing and daily life (the COPD Assessment Test, CAT) and blood tests. Oncedaily
measurement of symptoms will be commenced (using the a 14item
validated tool, the Exacerbations of Chronic
Pu

Period 1

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

Blinding implementation details:

A double-blinded design has been adopted to provide the best possible evidence for the efficacy of metformin in this context by minimising the risk of bias. Blinding will be implemented by means of visually identical active and placebo treatments. Randomisation lists will be produced in advance by the drug manufacturer and will be provided to the sponsor / lead site Pharmacy department for the purposes of allocation and/or emergency unblinding

Arms

Are arms mutually exclusive?	Yes
Arm title	active

Arm description:

active

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

Dosage and administration details:

2000 mg Capsule

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

500mg oral

Number of subjects in period 1	active	Placebo
Started	34	18
Completed	34	18

Baseline characteristics

End points

End points reporting groups

Reporting group title	active
Reporting group description: active	
Reporting group title	Placebo
Reporting group description: -	

Primary: Primary

End point title	Primary
End point description:	
End point type	Primary
End point timeframe: Mean capillary glucose concentration during hospitalisation period—defined as the mean of all capillary glucose measurements obtained according to the study protocol for that patient during the period between enrolment in the trial and hospital discharge.	

End point values	active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	18		
Units: 00				
arithmetic mean (full range (min-max))	00 (00 to 00)	00 (00 to 00)		

Statistical analyses

Statistical analysis title	Primary End-Point
Comparison groups	Placebo v active
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.273
Method	Not known

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Within 24 hours to the sponsor and CI from becoming aware	
Assessment type	Systematic

Dictionary used	
Dictionary name	SmPC
Dictionary version	0

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

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 Event data can be viewed in the End of Trial Report.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2010	Substantial amendment 1 - Changes made in relation to conditions specified by the REC in the REC approval letter dated 16th September 2010. - Additional site at Chelsea & Westminster Hospital added - The definition of severe sepsis as an exclusion criterion and as a treatment suspension criterion has been modified. - Changes have been made to the randomisation procedure and emergency unblinding in the protocol - Additional study assessments have been included: Monocyte-platelet aggregates Bacterial metagenomic analysis from a buccal (mouth) swab sample
19 January 2011	Substantial amendment 219 January 2011 - Minor changes made to the simplified IMPD to remove reference to the study protocol. This is to avoid having to amend the sIMPD every time we amend the study protocol and consequently change its version number. - Randomisation amended in protocol to blocks of 4 for C&W and blocks of 6 for SGUL - Pharmacovigilance section amended regarding wording and reporting requirements
22 August 2011	Substantial amendment 322 August 2011 Substantial Amendment 3 first submitted to REC and MHRA on 22 August 2011 with the following major changes: 1. Inclusion/exclusion criteria amended: 1.1. Inclusion criterion 4 (able to enter the study within 48 hours of admission) has been amended as the study team have found this criterion quite restrictive, precluding study entry for a significant proportion of patients screened. 1.2. The definition of exclusion criterion 4 (acute coronary syndrome), has been updated to accomodate the introduction of fondaparinux in place of dalteparin in the treatment of this condition. 2. The 'monocyte-platelet aggregates' assessment has been removed as it was not possible to establish the necessary laboratory assay. 3. The upper limit for the acceptable plasma lactate concentration has been increased from 2.7 to 3.0 mmol/L. 4. The requirement that study therapy be stopped pre-emptively in patients requiring a radiological examination with the administration of intravenous contrast has been removed 5. Addition of 4 new sites – Conquest Hospital, Hastings, Freeman Hospital, Notting ham, North Tees and New Castle 6. We would like to extend the study end date to 31st December 2012. 7. Change of PI at St George's from Dr Andrew Hitchings to Professor Emma Baker MHRA rejected first submission on 26/09/2011 with GNA. Resubmitted to MHRA on 04th October 2011 & REC on 06th October 2011 with further change in protocol to include the foll: "Retention of a requirement to suspend metformin before administration of intravascular iodinated contrast agent and that it not be reinstituted until 48 hours afterwards and only after renal functions has been re-evaluated and found to be normal' as per SmPC."

29 June 2012	Substantial amendment 429th June 2012 1. The active: placebo allocation ratio will increase from 1: 1 to 2:1. Accordingly, the target sample size will increase from 46 to 69 participants.. 2. To accommodate 2:1 allocation, the randomisation block size will be fixed at 6. 3. The intention to explore feasibility, safety and tolerability of the investigational treatment will be made explicit. 4. The secondary exploratory endpoints based on collection of a buccal swab and performance of the McKenzie skin blanch test will be removed, as it has not proved feasible to perform these tests with sufficient reliability. 5. The number of missed capillary glucose concentration measurements (≥3 out of 7 in a calendar day), or the maximum interval between consecutive measurements (>12 h), that will constitute a protocol deviation shall be defined. 6. Recurrence of COPD exacerbation will be added as a Protocol Defined Event, as it is a common event in the population under study, and contributes to the secondary analysis. 7. Change of sponsor contact from Ira Jakupovic (Clinical R&D Manager) to Nicki Collins (Sponsor representative). The Participant Information Leaflet, Informed Consent Form and GP Letter have been updated due to the changes in the protocol and also submitted for your review in tracked and clean versions.
03 April 2013	Substantial amendment 503rd April 2013 • 1. Adding new sites in uk · 2. Extending the recruitment period 3. A typographical error has been correct in the introductory section 4. Definitions for 'expectedness' have been updated to align with standard regulatory framework 5. The interpretation of Protocol Defined Events has been clarified 6. Fructosamine concentration has been added as a secondary endpoint 7. The terms used for sampling time-points have been standardised within the protocol 8. Reference to a Trial Management Group has been removed, as in practice, its membership and function has become the same as that of the Trial Steering Committee · 9. Updating GP letter in light of these changes · 10. Change of sponsor representative to Lucy Parker

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported