Clinical trial results:
A feasibility study investigating pravastatin for the prevention of preterm birth in women

Summary

EudraCT number	2017-005021-21
Trial protocol	GB
Global end of trial date	31 October 2020

Results information

Result version number	v1 (current)
This version publication date	22 February 2021
First version publication date	22 February 2021
Summary attachment (see zip file)	PIPIN REPORT 23DEC2020 (Clinical Study Report_PIPIN_Version 2.0 ETHICS 23DEC2020.doc)

Trial information

Trial identification

Sponsor protocol code	PIPIN

Additional study identifiers

ISRCTN number	ISRCTN82984919
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Ethics: 18/ES/0007, Sponsors references: AC17099, CSO Funders reference: TCS/18/30

Notes:

Sponsors

Sponsor organisation name	The University of Edinburgh & Lothian Health Board
Sponsor organisation address	ACCORD OFFICE, QMRI, 47 Little France Cresent, Edinburgh, United Kingdom, EH16 4TJ
Public contact	Sonia Whyte, University of Edinburgh, +44 131 242 2693, sonia.whyte@ed.ac.uk
Scientific contact	Sonia Whyte, University of Edinburgh, +44 131 242 2693, sonia.whyte@ed.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	30 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2019
Global end of trial reached?	Yes
Global end of trial date	31 October 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Feasibility study: This study is testing whether women between 28+0 and 35+6 weeks pregnant who come to hospital with signs and/or symptoms of preterm labour would be willing to take a medication (pravastatin) or placebo in a blinded fashion for 7 days.

Protection of trial subjects:

Participants were offered a information by a member of their clinical care team at the time of presentation. Women presenting with sign of preterm labour are often anxious and consideration was provided to ensure that they had time to consider participation. Whilst the nature of the intervention is time-critical, they will of course be offered as long as required to consider participation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2018
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: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Seven women were recruited from a single UK participating site. Women were identified in an antenatal care setting after they had presented with symptoms of preterm labour. Recruitment commenced 03rd August 2018 and the last patient visit was 29th November 2019

Pre-assignment

Screening details:

Patient eligibility was assessed by research staff, following identification of patients by clinical staff. Of the 214 patients screened, 35 (16%; 95% CI 11.7-22.0) were found to be eligible. Of the 35 eligible participants, 27 (77%) had a positive fetal fibronectin, whilst 8 (23%) had a cervical dilation ≥ 3cm.

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	Investigator, Monitor, Data analyst, Subject

Blinding implementation details:

IMP supplies were purchased and repackaged by GMP compliant company ISG (Investigational Supplies Group) who performed over encapsulation of the pravastatin, and prepared the placebo to be used. Randomisation codes were supplied to ISG separately by an independent member of the Edinburgh Clinical Trials Team. Pharmacy were supplied with sealed unblinding envelopes. No women were unblinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pravastatin Sodium 40mg tablets

Arm description:

The IMP (Pravastatin 40mg) will be manufactured by: Teva UK Limited and supplied to ISG (Investigational Supplies Group) who will performed over encapsulation of the pravastatin.

Arm type	Active comparator
Investigational medicinal product name	Pravastatin Sodium 40mg tablets
Investigational medicinal product code	PL-00289/0409
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

40mg Orally 1 dose per 24 hour period +/- 6 hours for a total of 7 days.

Arm title	Placebo

Arm description:

Matching Placebo

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

Dosage and administration details:

The principal excipient in pravastatin sodium is Lactose monohydrate 286.62mg, this will be used for the placebo. It will be formulated into a Swedish Orange hard gelatin capsule, size 00.

Number of subjects in period 1	Pravastatin Sodium 40mg tablets	Placebo
Started	3	4
Completed	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
Pregnant women	

Reporting group values	Overall Trial	Total	
Number of subjects	7	7	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	23.75		
full range (min-max)	18 to 29	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	0	0	

End points

End points reporting groups

Reporting group title	Pravastatin Sodium 40mg tablets

Reporting group description:

The IMP (Pravastatin 40mg) will be manufactured by: Teva UK Limited and supplied to ISG (Investigational Supplies Group) who will performed over encapsulation of the pravastatin.

Reporting group title	Placebo

Reporting group description:

Matching Placebo

Primary: Latency to Delivery

End point title	Latency to Delivery

End point description:

End point type	Primary

End point timeframe:

Time from presentation to acute care and assessment services with suspected preterm delivery to delivery itself (Latency to Delivery), as well as gestation at delivery

End point values	Pravastatin Sodium 40mg tablets	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: days	357	645		

Statistical analyses

Statistical analysis title	Methods

Statistical analysis description:

As this is a feasibility study, the quantitative data will be presented descriptively, using appropriate summary statistics with corresponding 95% confidence intervals. Additionally, the results will be summarised separately for the two population groups, and no formal comparisons will be made.

Comparison groups	Pravastatin Sodium 40mg tablets v Placebo
Number of subjects included in analysis	7
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	above not applicable
Parameter estimate	Mean difference (final values)
Point estimate	95

Confidence interval	
level	95 %
sides	2-sided
lower limit	90
upper limit	100

Notes:

[1] - as above note

[2] - not applicable for this study

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All adverse events (AE) that occur after informed consent until Estimated Date of Delivery (EDD) t + 28 days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11

Frequency threshold for reporting non-serious adverse events: 1 %

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: Only 7 women participated numbers details are in the report attached there were no adverse events in the pravastatin group

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

PIPIN is a feasibility study, and by nature, sample sizes are small, limiting clinical conclusions that can be drawn from results.

Notes: