Clinical trial results:
Prolonged ENoxapariN in primarY percutaneous coronary intervention compared WIth Standard-of-carE therapy: Feasibility study (PENNYWISE Feasibility)

Summary

EudraCT number	2018-000774-30
Trial protocol	GB
Global end of trial date	09 March 2020

Results information

Result version number	v1 (current)
This version publication date	23 August 2023
First version publication date	23 August 2023
Summary attachment (see zip file)	Prolonged enoxaparin therapy compared with standard-of-care antithrombotic therapy in opiate-treated patients undergoing primary percutaneous coronary intervention (Prolonged enoxaparin therapy compared with standard of care antithrombotic therapy in opiate treated patients undergoing primary percutaneous.pdf)

Trial information

Trial identification

Sponsor protocol code	STH19902

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03568838
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	8 Beech Hill Road, Sheffield, United Kingdom, S10 2SB
Public contact	Angela Pinder, Sheffield Teaching Hospitals NHS Foundation Trust, angela.pinder@nhs.net
Scientific contact	Angela Pinder, Sheffield Teaching Hospitals NHS Foundation Trust, angela.pinder@nhs.net

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	21 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2020
Global end of trial reached?	Yes
Global end of trial date	09 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a feasibility study with the objective to establish the practically possible recruitment rate into the study.
The other primary objective is to collect more pilot data on bleeding events within the first 24 hours and compare those between the two treatment arms.

Protection of trial subjects:

Study samples minimised to assess important endpoints but avoid undue discomfort.

Background therapy:

Dual antiplatelet therapy with a loading dose of 300mg of Aspirin and Ticagrelor or Prasugrel. All participants received Morphine or Diamorphine. 83% had received an antiemetic.

Evidence for comparator:

The comparator arm was Standard of Care in our institution.

Actual start date of recruitment	28 June 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: 100
Worldwide total number of subjects	100
EEA total number of subjects	0

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)	20

From 65 to 84 years	78
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment from 06/07/2018 to 09/03/2019, in a single UK centre.

Pre-assignment

Screening details:

During the screening period all patients attending the centre for Primary PCI were screened for eligibility to participate in the study, with an Investigator verbally consenting those eligible prior to their procedure as per the protocol. Written consent was subsequently achieved upon completion of the initial procedure at an appropriate time.

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	Enoxaparin

Arm description:

Patients randomised to Enoxaparin arm given 0.75mg/kg intraarterial bolus plus 0.75mg/kg intravenous infusion over 6 hours.

Arm type	Experimental
Investigational medicinal product name	Enoxaparin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intravenous bolus use , Intraarterial use

Dosage and administration details:

Enoxaparin 0.75mg/kg bolus plus 0.75mg/kg infusion over 6 hours.

Arm title	Unfractionated Heparin +/- Tirofiban

Arm description:

Standard of care for Primary PCI patients.

Arm type	Active comparator
Investigational medicinal product name	Unfractionated Heparin +/- Tirofiban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intraarterial use, Intravenous drip use

Dosage and administration details:

Unfractionated Heparin- 50-70iu/kg
Tirofiban- 25ug/kg for 3 minutes followed by 0.125ug/kg per minute for 6 hours.

Number of subjects in period 1	Enoxaparin	Unfractionated Heparin +/- Tirofiban
Started	50	50
Completed	50	49
Not completed	0	1
Adverse event, serious fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Enoxaparin
Reporting group description:	
Patients randomised to Enoxaparin arm given 0.75mg/kg intraarterial bolus plus 0.75mg/kg intravenous infusion over 6 hours.	
Reporting group title	Unfractionated Heparin +/- Tirofiban
Reporting group description:	
Standard of care for Primary PCI patients.	

Reporting group values	Enoxaparin	Unfractionated Heparin +/- Tirofiban	Total
Number of subjects	50	50	100
Age categorical			
Age of participant at time of consent.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	33	64
From 65-84 years	18	17	35
85 years and over	1	0	1
Gender categorical			
Units: Subjects			
Female	20	11	31
Male	30	39	69
Smoking Status			
Smoking status- current/past or none			
Units: Subjects			
None	17	13	30
Current/Past	33	37	70
Call to balloon time			
Units: minutes			
median	128	126	
inter-quartile range (Q1-Q3)	110 to 161	105 to 182	-

Subject analysis sets	
Subject analysis set title	Efficacy/safety analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomised participants who proceeded to angiography.	

Reporting group values	Efficacy/safety analysis set		
Number of subjects	99		
Age categorical			
Age of participant at time of consent.			
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)	63		
From 65-84 years	35		
85 years and over	1		
Gender categorical			
Units: Subjects			
Female	31		
Male	68		
Smoking Status			
Smoking status- current/past or none			
Units: Subjects			
None	30		
Current/Past	69		
Call to balloon time			
Units: minutes			
median	126		
inter-quartile range (Q1-Q3)	106 to 193		

End points

End points reporting groups

Reporting group title	Enoxaparin
Reporting group description:	
Patients randomised to Enoxaparin arm given 0.75mg/kg intraarterial bolus plus 0.75mg/kg intravenous infusion over 6 hours.	
Reporting group title	Unfractionated Heparin +/- Tirofiban
Reporting group description:	
Standard of care for Primary PCI patients.	
Subject analysis set title	Efficacy/safety analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomised participants who proceeded to angiography.	

Primary: Determine feasibility of conducting a bigger study

End point title	Determine feasibility of conducting a bigger study[1]
End point description:	
Recruitment rate over the study period.	
End point type	Primary
End point timeframe:	
Duration of study.	

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: The study protocol stated that the intention of this feasibility study was to determine potential recruitment rate. The recruitment target was met well within 1 year, supporting further studies of this type.

End point values	Enoxaparin	Unfractionated Heparin +/- Tirofiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: Number enrolled	50	49		

Statistical analyses

No statistical analyses for this end point

Primary: Collect pilot data on bleeding events

End point title	Collect pilot data on bleeding events[2]
End point description:	
Collect pilot data on bleeding events within the first 24 hours post procedure and compare between the two treatment arms. Trivial bleeding related to access site disregarded. Bleeding events will be categorised according to BARC types BARC2 - BARC5.	
End point type	Primary
End point timeframe:	
Bleeding rates at 24 hour timepoint.	

Notes:

[2] - 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: three bleeding events were recorded. One BARC2 event in the SOC group and two BARC1 events in the experimental group

End point values	Enoxaparin	Unfractionated Heparin +/- Tirofiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: absolute number	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Acute stent thrombosis rate

End point title	Acute stent thrombosis rate

End point description:

Acute stent thrombosis rates within the first 24 hours post procedure will be recorded for each treatment arm, and the two groups compared.

End point type	Secondary

End point timeframe:

Within first 24 hours post procedure.

End point values	Enoxaparin	Unfractionated Heparin +/- Tirofiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: absolute number	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of ST segment resolution

End point title	Rate of ST segment resolution

End point description:

Rates of ST-segment resolution will be calculated by comparing the presentation ECG and the ECG taken 1hr post procedure. The rates of ST-segment resolution will be compared between the two treatment groups.

End point type	Secondary

End point timeframe:

Rate of ST-segment resolution will be calculated using the presentation ECG and 1hr post PPCI ECG.

End point values	Enoxaparin	Unfractionated Heparin +/- Tirofiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: percentage resolution				
number (not applicable)	50	49		

Statistical analyses

Statistical analysis title	Percentage resolution
Statistical analysis description:	
Percentage ST segment resolution within 1 hour following primary percutaneous intervention	
Comparison groups	Enoxaparin v Unfractionated Heparin +/- Tirofiban
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.44 [3]
Method	Chi-squared
Parameter estimate	Median difference (final values)
Notes:	
[3] - no significant difference between groups	

Secondary: Rates of composite outcome of myocardial infarction

End point title	Rates of composite outcome of myocardial infarction
End point description:	
Rates of the composite outcome of recurrent myocardial infarction, ischaemic stroke or cardiovascular death within 30 days of STEMI will be recorded, and the two treatment groups compared.	
End point type	Secondary
End point timeframe:	
Within 30 days of STEMI	

End point values	Enoxaparin	Unfractionated Heparin +/- Tirofiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: absolute number	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: 1 year mortality rates

End point title	1 year mortality rates

End point description:

1 year mortality rates will be compared between the two groups.

End point type	Secondary

End point timeframe:

1 year post procedure

End point values	Enoxaparin	Unfractionated Heparin +/- Tirofiban		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: absolute number	3	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be reported from randomisation until 24 hours post PPCI for all participants in this study. Any AE deemed an SAE will be reported to the sponsor within 24 hours of the study team becoming aware.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Unfractionated Heparin +/- Tirofiban

Reporting group description:

Participants presenting with STEMI treated with an opiate were randomised to standard of care. This group received treatment at the discretion of their cardiologist consisting of a weight adjusted bolus dose of UFH 50-70 IU/kg + a 6 hour regimen of tirofiban (or UFH 70 IU/kg alone if concerns about bleeding risk). The tirofiban regimen consisted of 25 mcg/kg over 3 mins (or 6 mins if weight > 120kg) followed by maintenance dose of 0.15 mcg/kg/min for patients with eGFR more than or equal to 30ml/min/1.73m2 for 6 hours. Half of the aforementioned tirofiban doses were used for patients with an eGFR less than 30 mcg/kg/1.73m2.

Reporting group title	Enoxaparin

Reporting group description:

Participants presenting with STEMI who had been treated with opiates randomised to receive an intra-arterial bolus (0.75mg/kg) of enoxaparin followed by intravenous infusion of enoxaparin 0.75mg/kg/6 hours.

Serious adverse events	Unfractionated Heparin +/- Tirofiban	Enoxaparin	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 49 (4.08%)	0 / 50 (0.00%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	0	
Cardiac disorders			
Coronary stent thrombosis			
subjects affected / exposed	2 / 49 (4.08%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Unfractionated Heparin +/- Tirofiban	Enoxaparin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 49 (2.04%)	2 / 50 (4.00%)	
General disorders and administration site conditions			
Gingival bleeding			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
GI bleed	Additional description: upper GI bleed		
subjects affected / exposed	0 / 49 (0.00%)	2 / 50 (4.00%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 50 (2.00%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
rash	Additional description: Rash on torso		
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32543247