



Clinical trial results:

Prolonged ENoxaparin in primary Percutaneous Coronary Intervention; a Pilot Pharmacodynamic study (PENNY PCI study)

Summary

EudraCT number	2017-000485-29
Trial protocol	GB
Global end of trial date	30 March 2018

Results information

Result version number	v1 (current)
This version publication date	08 November 2018
First version publication date	08 November 2018

Trial information

Trial identification

Sponsor protocol code	STH19752
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03146858
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS FT
Sponsor organisation address	Glossop Road, Sheffield, United Kingdom, S10 2JF
Public contact	Nana Theodorou, STH NHS FT, 0114 2712763, nana.theodorou@sth.nhs.uk
Scientific contact	Nana Theodorou, STH NHS FT, 0114 2712763, nana.theodorou@sth.nhs.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	31 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2017
Global end of trial reached?	Yes
Global end of trial date	30 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to study the pharmacodynamic effects of a novel regimen of enoxaparin (a bolus followed by an infusion) in patients presenting with STEMI. The primary outcome measure was anti Xa activity. The aim of this regimen is to offer sufficient antithrombotic effect in order to bridge treatment with oral therapy.

Protection of trial subjects:

The trial protocol has been independently reviewed.

All approvals were obtained before commencing recruitment. Study was completed according to the principles set in Good Clinical Practice.

Background therapy:

Not applicable as there was no requirements for the patient to be on any other drugs.

Evidence for comparator: -

Actual start date of recruitment	12 June 2017
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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	11
From 65 to 84 years	11

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Potential participants were identified by the clinical team directly involved in their care. Upon identification of eligible patients, the clinical research team was informed.

Pre-assignment

Screening details:

Each patient entering the study was screened for all of the inclusion criteria and had none of the exclusion criteria. The Principal Investigator or a medically qualified co investigator will confirm eligibility for the study. All the exclusion criteria are usually checked routinely as part of routine clinical practice.

Period 1

Period 1 title	Medication period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Enoxaparin
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Arm description:

Bolus followed by infusion intraarterial enoxaparin

Arm type	Experimental
Investigational medicinal product name	Enoxaparin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Anticoagulant and preservative solution for blood
Routes of administration	Intracoronary use, Intravenous use

Dosage and administration details:

A bolus of IA/IV enoxaparin 0.75 mg/kg (pre PCI) followed by an IV infusion of 0.75 mg/kg over 6 hours.

Number of subjects in period 1	Enoxaparin
Started	22
Completed	19
Not completed	3
Physician decision	1
Received different treatment to latest protocol	2

Baseline characteristics

Reporting groups

Reporting group title	Medication period
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Reporting group description:

The protocol was amended after the second patient as anti Xa levels were found to be low (0.51 IU/ml). Results reported in this report are for the 20 patients who received the updated protocol recommended treatment (0.75 mg/kg of IA enoxaparin followed by 0.75 mg/kg/6h infusion).

Reporting group values	Medication period	Total	
Number of subjects	22	22	
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	66.2		
standard deviation	± 10.7	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	18	18	

Subject analysis sets

Subject analysis set title	Pharmacodynamic analysis
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Subject analysis set type	Per protocol
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Subject analysis set description:

All enrolled patients that received enoxaparin for the dose and duration specified in the latest version of the protocol

Reporting group values	Pharmacodynamic analysis		
Number of subjects	19		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	67.0 ± 10.8		
Gender categorical Units: Subjects			
Female Male	3 16		

End points

End points reporting groups

Reporting group title	Enoxaparin
Reporting group description: Bolus followed by infusion intraarterial enoxaparin	
Subject analysis set title	Pharmacodynamic analysis
Subject analysis set type	Per protocol
Subject analysis set description: All enrolled patients that received enoxaparin for the dose and duration specified in the latest version of the protocol	

Primary: Anti-Xa activity

End point title	Anti-Xa activity
End point description:	
End point type	Primary
End point timeframe: Time point 1 (T1) prior to anticoagulation – at the start of PCI procedure. Time point 2 (T2) at the end of PPCI. Time point 3 (T3) 2-3 hours from the start of enoxaparin infusion. Time point 4 (T4) at the end of enoxaparin infusion.	

End point values	Enoxaparin	Pharmacodynamic analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	19 ^[1]	19		
Units: iu/ml				
arithmetic mean (standard deviation)	1.003 (± 0.06)	1.003 (± 0.06)		

Notes:

[1] - Reporting the primary end point after 6 hours

Statistical analyses

Statistical analysis title	ANOVA
Statistical analysis description: One-way analysis of variance (ANOVA) was used for assessment of continuous variables. Variance during the infusion was assessed using one-way analysis of variance (ANOVA) with Dunnett's multiple comparison tests . Six hours versus 2 to 3 hours; p=0.6 and 6 hours versus post-PCI; p=0.09	
Comparison groups	Enoxaparin v Pharmacodynamic analysis
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.09 ^[2]
Method	ANOVA
Parameter estimate	Mean difference (net)

Notes:

[2] - 6 hours versus post-PCI; $p=0.09$

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

14 hours after the start of the infusion

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20
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Reporting groups

Reporting group title	Pharmacodynamic set
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Reporting group description: -

Reporting group title	Medication arm
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Reporting group description:

The 22 subjects enrolled

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: In this study there were no reported non-serious adverse events.

Serious adverse events	Pharmacodynamic set	Medication arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
10063933			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pharmacodynamic set	Medication arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2017	Temporary halt
17 July 2017	SA02 to update proctol and re start the trial

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 June 2017	The second patient suffered a stent thrombosis in the context of a long segment of underdeployed stent. DMC were informed and we halted the trial. Anti Xa levels were 0.51 IU/ml. We therefore increased the enoxaparin dose to 0.75 mg/kg bolus followed by 0.75 mg/kg/6h infusion.	25 August 2017

Notes:

Limitations and caveats

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

The protocol was amended after the second patient as anti Xa levels were found to be low (0.51 IU/ml). Results reported in this report are for the 20 patients who received the updated protocol recommended treatment (0.75 mg/kg of IA enoxaparin follow

Notes: