Clinical trial results:
A feasibility study to inform the design of a randomised controlled trial to identify the most clinically and cost effective length of Anticoagulation with Low molecular weight heparin In the treatment of Cancer Associated Thrombosis (ALICAT).

Summary

EudraCT number	2012-004117-14
Trial protocol	GB
Global end of trial date	22 November 2014

Results information

Result version number	v1 (current)
This version publication date	30 March 2019
First version publication date	30 March 2019
Summary attachment (see zip file)	Full HTA report (FullReport-hta19830.pdf)

Trial information

Trial identification

Sponsor protocol code	SPON1037-11

Additional study identifiers

ISRCTN number	ISRCTN37913976
ClinicalTrials.gov id (NCT number)	NCT01817257
WHO universal trial number (UTN)	-
Other trial identifiers	WCTU Number: WCTU062, Sponsors Number: SPON1037-11, NIHR HTA Project Reference Number: 10/145/01

Notes:

Sponsors

Sponsor organisation name	Cardiff University
Sponsor organisation address	30-36 Newport Road, Cardiff, United Kingdom, CF24 0DE
Public contact	Shaw, Cardiff University, +44 29 2087 5834/9626, shawc3@cardiff.ac.uk
Scientific contact	Shaw, Cardiff University, +44 29 2087 5834/9626, shawc3@cardiff.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	10 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 November 2014
Global end of trial reached?	Yes
Global end of trial date	22 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To explore the feasibility of conducting a randomised controlled trial (RCT) to identify the use of low molecular weight heparin (LMWH) in the treatment of cancer associated thrombosis (CAT) in patients with locally advanced or metastatic cancer following an initial six months of anticoagulation.

Protection of trial subjects:

It was anticipated that participants may prefer one randomization arm to the other. As such participants were asked to participate in qualitative interviews and quality of life questionnaires. Furthermore, as participants would be asked to self-inject, xxxxx were designed to look into participants feelings and preferences relating to this.

Background therapy:

Cancer patients are at higher risk of Venous thromboembolism (VTE). It is therefore recommended that patients receive Low molecular weight heparin (LMWH) for six months only.

Evidence for comparator:

It is unknown whether treating patients with LMWH for longer would improve patient outcomes, particularly for patients with cancer associated thrombosis (CAT) and ongoing cancer whereby the risk of thrombotic tendency increases.

Actual start date of recruitment	03 June 2013
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: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	3
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first participants was registered on the 23/12/2013 and the last participant was registered on the 16/06/2014. Participants were registered across 2 UK sites.

Pre-assignment

Screening details:

Index VTE events were identified through primary and secondary care clinical databases and clinical records. Potential participants were screened by a NISCHR (Welsh sites) or NIHR NCRN (English sites) researcher and flagged up to the local PI.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	LMWH 12 months

Arm description:

Participants receive 12 months of LMWH.

Arm type	Experimental
Investigational medicinal product name	LMWH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

As per local policy. LMWH may include dalteparin (Fragmin®),tinzaparin (Innohep®) and enoxaparin (Clexane®)

Arm title	LMWH for 6 months

Arm description:

Participants receive 6 months of LMWH only.

Arm type	Experimental
Investigational medicinal product name	LMWH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

As per local policy. Permitted LMWH include dalteparin (Fragmin®), tinzaparin (Innohep®) and enoxaparin (Clexane®)

Number of subjects in period 1	LMWH 12 months	LMWH for 6 months
Started	3	2
Completed	2	1
Not completed	1	1
Patient died	1	1

Baseline characteristics

Reporting groups	
Reporting group title	LMWH 12 months
Reporting group description:	
Participants receive 12 months of LMWH.	
Reporting group title	LMWH for 6 months
Reporting group description:	
Participants receive 6 months of LMWH only.	

Reporting group values	LMWH 12 months	LMWH for 6 months	Total
Number of subjects	3	2	5
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			
Mean age			
Units: years			
arithmetic mean	66.67	50.5	
standard deviation	± 11.93	± 21.92	-
Gender categorical Units: Subjects			
Female	1	1	2
Male	2	1	3
ECOG Performance status Units: Subjects			
ECOG 0	2	2	4
ECOG 2	1	0	1

Subject analysis sets	
Subject analysis set title	Overall Trial
Subject analysis set type	Full analysis
Subject analysis set description:	
All 5 patients who were randomised.	

Reporting group values	Overall Trial		
Number of subjects	5		
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			
Mean age			
Units: years arithmetic mean standard deviation	±		
Gender categorical Units: Subjects			
Female Male	2 3		
ECOG Performance status Units: Subjects			
ECOG 0 ECOG 2	4 1		

End points

End points reporting groups

Reporting group title	LMWH 12 months
Reporting group description:	
Participants receive 12 months of LMWH.	
Reporting group title	LMWH for 6 months
Reporting group description:	
Participants receive 6 months of LMWH only.	
Subject analysis set title	Overall Trial
Subject analysis set type	Full analysis
Subject analysis set description:	
All 5 patients who were randomised.	

Primary: (i) Number of eligible patients

End point title	(i) Number of eligible patients[1]
End point description:	
A screening log will be kept in each recruitment site to identify patients potentially meeting the inclusion criteria. Eligible patients who are approached about the trial and given the participant information sheet (PIS) will be anonymously registered on a central database. This will help to inform the design of a Phase III study.	
End point type	Primary
End point timeframe:	
The sites were open for recruitment for 6 months between December 2013 and June 2014	

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: Only 5 out of 32 (15.6%) eligible patients agreed to be randomised. The study was closed early the primary outcome was feasibility of randomisation.

End point values	Overall Trial			
Subject group type	Subject analysis set			
Number of subjects analysed	32[2]			
Units: Patients	32			

Notes:

[2] - 32 patients were registered as potentially eligible.

Statistical analyses

No statistical analyses for this end point

Primary: (ii) Number of recruited patients

End point title	(ii) Number of recruited patients[3]
End point description:	
Patients meeting the inclusion criteria will be invited to participate in the study as outlined. The number of eligible participants consenting to randomisation shall be recorded.	
End point type	Primary
End point timeframe:	
The sites were open for recruitment for 6 months between December 2013 and June 2014	

Notes:

[3] - 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: Only 5 out of 32 (15.6%) eligible patients agreed to be randomised. The study was closed early the primary outcome was feasibility of randomisation.

End point values	Overall Trial			
Subject group type	Subject analysis set			
Number of subjects analysed	5[4]			
Units: Patients	5			

Notes:

[4] - 5 patients were randomised

Statistical analyses

No statistical analyses for this end point

Primary: (iii) Proportion of randomised participants with recurrent VTEs during follow-up

End point title	(iii) Proportion of randomised participants with recurrent VTEs during follow-up[5]

End point description:

The number of randomised patients experiencing recurrent symptomatic VTE shall be recorded and used to inform the sample size required for a full RCT.

End point type	Primary

End point timeframe:

6 month trial follow-up period

Notes:

[5] - 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: Only 5 out of 32 (15.6%) eligible patients agreed to be randomised. The study was closed early the primary outcome was feasibility of randomisation.

End point values	Overall Trial			
Subject group type	Subject analysis set			
Number of subjects analysed	32[6]			
Units: Number of patients randomised				
randomised	5			
not randomised	27			

Notes:

[6] - 32 patients registered.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were reported from time of signature of informed consent, throughout the treatment period up to, and including 30 days after the participant receives their last dose of the IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Patients treated with LMWH for 12 months
Reporting group description: -	
Reporting group title	Patients treated with LMWH for 6 months

Reporting group description: -

Serious adverse events	Patients treated with LMWH for 12 months	Patients treated with LMWH for 6 months	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	1 / 2 (50.00%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Fall			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colonic obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary tract obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Community acquired pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Patients treated with LMWH for 12 months	Patients treated with LMWH for 6 months	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	1 / 2 (50.00%)	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	2 / 3 (66.67%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Transient elevation of liver transaminases			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Raised Gamma GT			

subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash, urticarial, Pruritus			
subjects affected / exposed	2 / 3 (66.67%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Subcataneous haematoma at injection site			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Sore mouth			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
urinary catheter			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2014	The ALICAT Protocol was updated from V2.0 21 March 2013 to V2.1 20 November 2013 to reflect changes to the WCTU's generic pharmacovigilance management, assessment and reporting procedures in response to a Statutory GCP Systems Inspection (INSPECTION No: Insp GCP 21323/8955167-0001) of the WCTU conducted by the MHRA 20-22 August 2013. Other minor typographical amendments to the protocol were addressed at the same time.
17 March 2014	Addition of new site(s) and/or investigator(s)
27 May 2014	Amendment of the ALICAT Protocol from V2.1 to V3.0; Comments/ explanation/ reasons for substantial amendment: 1. Remove reference to recruitment of patients to the RCT and qualitative interviews from the primary care setting, i.e. GP sites, and clarify that patients will be recruited from five participating hospital sites (two for the oncology setting in Wales and three for the haematology setting in England) 2. Remove reference to a Researcher at Birmingham University. 3. Reduce the current 16 RSIs to three, i.e. one per active ingredient. 4. Specify that one DSUR will be submitted for all three active ingredients. 5. Clarification of the conduct of the patient mapping component of the study. 6. Other minor typographical errors. Notification on to REC only of removal of the ALICAT Consultant Letter Version 1.0 160112. This document was no longer required as patients were no longer recruited from the primary care setting. Amendment to the ALICAT PIS and consent forms to address minor typographical errors, and reflect changes to the design of the focus group component of the study following implementation of the first three focus groups.

Notes:

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.

Low recruitment and randomisation numbers suggest progression to a full RTC was not feasible. Reasons for non-consenting were due to fixed preference for continuing or discontinuing treatment after 6 months of LMWH.

Notes: