



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 | 2 | | |
| Male | 3 | | |
| ECOG Performance status | | | |
| Units: Subjects | | | |
| ECOG 0 | 4 | | |
| ECOG 2 | 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 occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 2 (50.00%) 1 | |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 2 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Rash, urticarial, Pruritus subjects affected / exposed occurrences (all) Subcutaneous haematoma at injection site subjects affected / exposed occurrences (all) Sore mouth subjects affected / exposed occurrences (all) | 2 / 3 (66.67%) 2 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 1 / 2 (50.00%) 2 | |
| Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all) urinary catheter subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 | 0 / 2 (0.00%) 0 1 / 2 (50.00%) 1 | |
| Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 2 (0.00%) 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 | <p>Amendment of the ALICAT Protocol from V2.1 to V3.0; Comments/ explanation/ reasons for substantial amendment:</p> <ol style="list-style-type: none">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. <p>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.</p> <p>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.</p> |

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: