



Clinical trial results:

The role of apixaban, aspirin and enoxaparin as Thromboprophylaxis in patients newly diagnosed with Multiple Myeloma - an open label randomised control clinical trial

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-002668-18 |
| Trial protocol | GB |
| Global end of trial date | 27 June 2017 |

Results information

| | |
|-----------------------------------|------------------------------------|
| Result version number | v1 (current) |
| This version publication date | 15 March 2019 |
| First version publication date | 15 March 2019 |
| Summary attachment (see zip file) | FINAL STUDY REPORT (TiMM1 V4.docx) |

Trial information

Trial identification

| | |
|-----------------------|------|
| Sponsor protocol code | TiMM |
|-----------------------|------|

Additional study identifiers

| | |
|------------------------------------|------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | REC number: 15/LO/1319 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | King's College Hospital NHS Foundation Trust |
| Sponsor organisation address | Denmark Hill, London, United Kingdom, SE5 9RS |
| Public contact | Professor Roopen Arya, King's College Hospital NHS Foundation Trust, +44 02032993570, roopen.arya@nhs.net |
| Scientific contact | Professor Roopen Arya, King's College Hospital NHS Foundation Trust, +44 02032993570, roopen.arya@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 | 27 June 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 June 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 June 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Safety of apixaban as a thromboprophylactic agent in the newly diagnosed myeloma population

Protection of trial subjects:

Patients are free to withdraw consent for study treatment and/or consent to participate in the study at any time and without the prejudice to further treatment. Patients who withdraw from study treatment, but are willing to continue to participate in the follow-up visits should be followed according to the procedures outlined in the protocol.

Background therapy:

For the low risk group, aspirin 75mg tablets (once tablet once a day) or apixaban 2.5mg tablets (one tablet twice a day) will be prescribed for patients, according to which arm they are randomised to. For the high risk group, enoxaparin 40mg daily* (by subcutaneous once a day) or apixaban 2.5mg tablets (one tablet twice a day) will be prescribed for patients, according to which arm they are randomised to.

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 09 May 2016 |
| 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: 10 |
| Worldwide total number of subjects | 10 |
| EEA total number of subjects | 10 |

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) | 5 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were recruited between 12/04/2016 and 21/04/2017. Participants were recruited from King's College Hospital NHS Foundation Trust

Pre-assignment

Screening details:

Patients with newly diagnosed with multiple myeloma requiring chemotherapy, age >18 years and able to give informed consent were recruited. 29 patients were screened.

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 10 |
| Number of subjects completed | 10 |

Period 1

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

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | High risk apixaban |

Arm description:

Newly diagnosed multiple myeloma patients with a high risk of developing a venous thromboembolic event randomised to receive apixaban

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Apixaban |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg milligram(s) per day

| | |
|------------------|------------------------|
| Arm title | Standard risk apixaban |
|------------------|------------------------|

Arm description:

Newly diagnosed multiple myeloma patients with a standard risk of developing a venous thromboembolic event randomised to receive apixaban

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Apixaban |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg milligram(s) per day

| | |
|------------------|-----------------------|
| Arm title | Standard risk aspirin |
|------------------|-----------------------|

Arm description:

Newly diagnosed multiple myeloma patients with a standard risk of developing a venous

thromboembolic event randomised to receive aspirin

| | |
|--|--------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Aspirin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

75 mg milligram(s) per day

| Number of subjects in period 1 | High risk apixaban | Standard risk apixaban | Standard risk aspirin |
|---------------------------------------|--------------------|------------------------|-----------------------|
| Started | 2 | 4 | 4 |
| Completed | 1 | 3 | 1 |
| Not completed | 1 | 1 | 3 |
| Adverse event, non-fatal | 1 | 1 | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Overall trial period |
|-----------------------|----------------------|

Reporting group description:

Newly diagnosed multiple myeloma patients were recruited between the ages 50 and 79.

| Reporting group values | Overall trial period | Total | |
|--|----------------------|-------|--|
| Number of subjects | 10 | 10 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 50-59 years | 3 | 3 | |
| 60-69 years | 4 | 4 | |
| 70-79 years | 3 | 3 | |
| Gender categorical | | | |
| Both male and female subjects were recruited for this trial. | | | |
| Units: Subjects | | | |
| Female | 5 | 5 | |
| Male | 5 | 5 | |

End points

End points reporting groups

| | |
|---|------------------------|
| Reporting group title | High risk apixaban |
| Reporting group description: Newly diagnosed multiple myeloma patients with a high risk of developing a venous thromboembolic event randomised to receive apixaban | |
| Reporting group title | Standard risk apixaban |
| Reporting group description: Newly diagnosed multiple myeloma patients with a standard risk of developing a venous thromboembolic event randomised to receive apixaban | |
| Reporting group title | Standard risk aspirin |
| Reporting group description: Newly diagnosed multiple myeloma patients with a standard risk of developing a venous thromboembolic event randomised to receive aspirin | |

Primary: Safety of apixaban as a thromboprophylactic agent in the newly diagnosed myeloma population

| | |
|-----------------|--|
| End point title | Safety of apixaban as a thromboprophylactic agent in the newly diagnosed myeloma population ^[1] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Bleeding events were captured from 1st dose of IMP until 10 days post last dose of IMP.

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: No statistical tests were undertaken as the study is not powered to detect meaningful significance.

| End point values | High risk apixaban | Standard risk apixaban | Standard risk aspirin | |
|-----------------------------|--------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2 | 4 | 4 | |
| Units: Bleeding events | 0 | 2 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Venous Thromboembolic events

| | |
|-----------------|------------------------------|
| End point title | Venous Thromboembolic events |
|-----------------|------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Venous Thromboembolic events were captured from first dose of IMP until 10 days post last dose of IMP.

| End point values | High risk apixaban | Standard risk apixaban | Standard risk aspirin | |
|-----------------------------|-----------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2 | 4 | 4 | |
| Units: number of events | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Recruitment rate from eligible population to the stud

| | |
|-----------------|---|
| End point title | Recruitment rate from eligible population to the stud |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

12 month recruitment period

| End point values | High risk apixaban | Standard risk apixaban | Standard risk aspirin | |
|-------------------------------------|-----------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2 | 4 | 4 | |
| Units: Number of patients recruited | 2 | 4 | 4 | |

| | |
|-----------------------------------|----------------------------------|
| Attachments (see zip file) | FINAL STUDY REPORT/TiMM1 V4.docx |
|-----------------------------------|----------------------------------|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were reported from consent until 10 days after administration of the last dose of study medication

Adverse event reporting additional description:

Patients will be risked assessed for VTE, as soon as the treatment for the myeloma is initiated. For patients who consent to the study, they will be randomised to apixaban or aspirin and will continue this VTE preventative medication until they are deemed to be in remission.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | High risk apixaban |
|-----------------------|--------------------|

Reporting group description:

Newly diagnosed multiple myeloma patients with a high risk of developing a venous thromboembolic event randomised to receive apixaban

| | |
|-----------------------|------------------------|
| Reporting group title | Standard risk apixaban |
|-----------------------|------------------------|

Reporting group description:

Newly diagnosed multiple myeloma patients with a standard risk of developing a venous thromboembolic event randomised to receive apixaban

| | |
|-----------------------|-----------------------|
| Reporting group title | Standard risk aspirin |
|-----------------------|-----------------------|

Reporting group description:

Newly diagnosed multiple myeloma patients with a standard risk of developing a venous thromboembolic event randomised to receive aspirin

| Serious adverse events | High risk apixaban | Standard risk apixaban | Standard risk aspirin |
|---|--|------------------------|-----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 4 (25.00%) | 1 / 4 (25.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Myocardial infarction | Additional description: Chest pain and raised troponin | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 4 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---|----------------|----------------|
| Sepsis syndrome subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Non-neutropenic sepsis and toxic erythema | | |
| | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 1 / 4 (25.00%) |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Elevated blood glucose | | |
| | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 4 (0.00%) |
| | 0 / 0 | 0 / 1 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | High risk apixaban | Standard risk apixaban | Standard risk aspirin |
|--|---------------------|------------------------|-----------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 2 / 2 (100.00%) | 3 / 4 (75.00%) | 3 / 4 (75.00%) |
| Blood and lymphatic system disorders Cephalic vein thrombosis subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 1 / 4 (25.00%) 1 | 1 / 4 (25.00%) 1 |
| Bleeding subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 2 / 4 (50.00%) 2 | 1 / 4 (25.00%) 1 |
| General disorders and administration site conditions light headed subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 4 (0.00%) 0 |
| Eye disorders Chromatopsia subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 4 (0.00%) 0 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea | 1 / 2 (50.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |

| | | | |
|--|--|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Redness | Additional description: Red blotches on skin | | |
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back ache | | | |
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Bilateral calf tenderness | | | |
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Infections and infestations | | | |
| Raised temperature | | | |
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 |

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