



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
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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
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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
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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
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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]
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End point description:

End point type	Primary
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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
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	High risk apixaban
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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
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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
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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