Clinical trial results:
Magnetic Resonance Imaging Using Ultrasmall Superparamagnetic Particles of Iron Oxide in Patients Under Surveillance for Abdominal Aortic Aneurysms to Predict Rupture or Surgical Repair: the MA3RS Trial

Summary

EudraCT number	2012-002448-25
Trial protocol	GB
Global end of trial date	01 November 2016

Results information

Result version number	v1 (current)
This version publication date	30 May 2019
First version publication date	30 May 2019

Trial information

Trial identification

Sponsor protocol code	MA3RS Trial

Additional study identifiers

ISRCTN number	ISRCTN76413758
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The University of Edinburgh
Sponsor organisation address	Old College, South Bridge, Edinburgh, United Kingdom, EH8 9YL
Public contact	Professor David Newby, The University of Edinburgh, +44 0131 242 6515 , d.e.newby@ed.ac.uk
Scientific contact	Professor David Newby, The University of Edinburgh, +44 0131 242 6515 , d.e.newby@ed.ac.uk
Sponsor organisation name	Lothian Health Board
Sponsor organisation address	Waverley Gate, 2-4 Waterloo Place, Edinburgh, United Kingdom, EH1 3EG
Public contact	Professor David Newby, The University of Edinburgh, +44 0131 242 6515 , d.e.newby@ed.ac.uk
Scientific contact	Professor David Newby, The University of Edinburgh, +44 0131 242 6515 , d.e.newby@ed.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2016
Global end of trial reached?	Yes
Global end of trial date	01 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

An abdominal aortic aneurysm is a swelling of the main blood vessel that supplies the organs in the abdomen and the legs. It most commonly occurs just below the kidneys (approximately at the level of the belly button). It is not yet clear why some people develop aneurysms but they are more common in smokers and in men. Abdominal aortic aneurysms are dangerous because they can rupture and if this happens up to 90% of people affected will die. Of those who make it to hospital, they have a less than 50% chance of surviving. At present, we use size, measured by an ultrasound scan, to best predict which abdominal aortic aneurysms are most likely to rupture. The problem with this is that sometimes small abdominal aortic aneurysms rupture and large abdominal aortic aneurysms go on to grow to 10cm without rupturing. This suggests that size is not the only factor to cause abdominal aortic aneurysms to grow and rupture. The principal objective of this study is to use magnetic resonance

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2012
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: 342
Worldwide total number of subjects	342
EEA total number of subjects	342

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)	115
From 65 to 84 years	227
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was across 3 sites in Scotland, UK.
Recruitment opened in November 2012 and closed in December 2014.
There was a temporary halt on recruitment between July 2014 and September 2014 after an urgent update to administration guidelines of study drug

Pre-assignment

Screening details:

Patients were identified from the surveillance service database and eligibility was assessed either at the surveillance ultrasound appointment or over the telephone. Eligibility was confirmed before consent was taken.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All patients

Arm description:

All patients recruited

Arm type	Experimental
Investigational medicinal product name	Ferumoxytol
Investigational medicinal product code	NA
Other name	NA
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The single use vials are diluted and administered as an intravenous infusion over 15-30 minutes. The ferumoxytol dose (4.0 mg/kg) is diluted in sterile 0.9% sodium chloride up to a final concentration of 2-8 mg iron per mL.

Number of subjects in period 1	All patients
Started	342
Completed	342

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	342	342	
Age categorical Units: Subjects			
Age continuous Units: years			
median	74.0		
full range (min-max)	53.0 to 91.0	-	
Gender categorical Units: Subjects			
Female	50	50	
Male	292	292	
Smoking Status Units: Subjects			
Current	101	101	
Ex-smoker	195	195	
Never	46	46	
Alcohol intake Units: Subjects			
Missing	2	2	
Yes	134	134	
No	206	206	
CIA Units: Subjects			
No	276	276	
Right	21	21	
Left	10	10	
Both	35	35	
Hypertension Units: Subjects			
Yes	246	246	
No	96	96	
Diabetes Units: Subjects			
Yes	47	47	
No	295	295	
Hypercholesterolaemia Units: Subjects			
Yes	257	257	
No	85	85	
IHD			

Units: Subjects			
No	217	217	
Yes	125	125	
Angina Units: Subjects			
Yes	50	50	
No	292	292	
MI Units: Subjects			
Yes	92	92	
No	250	250	
PCI Units: Subjects			
Yes	34	34	
No	308	308	
CABG Units: Subjects			
Yes	42	42	
No	300	300	
PVD Units: Subjects			
No	276	276	
Yes	66	66	
PVD - Claudication Units: Subjects			
Yes	62	62	
No	280	280	
PVD - rest pain Units: Subjects			
Yes	2	2	
No	340	340	
PVD - tissue loss Units: Subjects			
Yes	2	2	
No	340	340	
PVD - angioplasty Units: Subjects			
Yes	11	11	
No	331	331	
PVD - bypass Units: Subjects			
Yes	8	8	
No	334	334	
CVD Units: Subjects			
No	296	296	
Yes	46	46	
CD TIA Units: Subjects			
Yes	28	28	
No	314	314	

CD CVA Units: Subjects			
Yes	19	19	
No	323	323	
Family History of AAA Units: Subjects			
Yes	61	61	
No	281	281	
ACE-1 Units: Subjects			
Yes	123	123	
No	219	219	
Anticoagulant Units: Subjects			
No	317	317	
Yes	25	25	
Antiplatlet Units: Subjects			
Yes	224	224	
No	118	118	
Beta blocker Units: Subjects			
Yes	120	120	
No	222	222	
Statin Units: Subjects			
No	72	72	
Yes	270	270	

Subject analysis sets

Subject analysis set title	All participants
Subject analysis set type	Full analysis

Subject analysis set description:

Consented patients who were non-withdrawn during baseline assessment phase

Reporting group values	All participants		
Number of subjects	342		
Age categorical Units: Subjects			

Age continuous Units: years			
median	74.0		
full range (min-max)	53.0 to 91.0		
Gender categorical Units: Subjects			
Female	50		
Male	292		

Smoking Status Units: Subjects			
Current	101		
Ex-smoker	195		
Never	46		
Alcohol intake Units: Subjects			
Missing	2		
Yes	134		
No	206		
CIA Units: Subjects			
No	276		
Right	21		
Left	10		
Both	35		
Hypertension Units: Subjects			
Yes	246		
No	96		
Diabetes Units: Subjects			
Yes	47		
No	295		
Hypercholesterolaemia Units: Subjects			
Yes	257		
No	85		
IHD Units: Subjects			
No	217		
Yes	125		
Angina Units: Subjects			
Yes	50		
No	292		
MI Units: Subjects			
Yes	92		
No	250		
PCI Units: Subjects			
Yes	34		
No	308		
CABG Units: Subjects			
Yes	42		
No	300		
PVD Units: Subjects			
No	276		

Yes	66		
PVD - Claudication Units: Subjects			
Yes No	62 280		
PVD - rest pain Units: Subjects			
Yes No	2 340		
PVD - tissue loss Units: Subjects			
Yes No	2 340		
PVD - angioplasty Units: Subjects			
Yes No	11 331		
PVD - bypass Units: Subjects			
Yes No	8 334		
CVD Units: Subjects			
No Yes	296 46		
CD TIA Units: Subjects			
Yes No	28 314		
CD CVA Units: Subjects			
Yes No	19 323		
Family History of AAA Units: Subjects			
Yes No	61 281		
ACE-1 Units: Subjects			
Yes No	123 219		
Anticoagulant Units: Subjects			
No Yes	317 25		
Antiplatlet Units: Subjects			
Yes No	224 118		
Beta blocker Units: Subjects			

Yes	120		
No	222		
Statin Units: Subjects			
No	72		
Yes	270		

End points

End points reporting groups

Reporting group title	All patients
Reporting group description:	
All patients recruited	
Subject analysis set title	All participants
Subject analysis set type	Full analysis
Subject analysis set description:	
Consented patients who were non-withdrawn during baseline assessment phase	

Primary: AAA Rupture and Repair

End point title	AAA Rupture and Repair[1]
End point description:	
Number of days between consent and rupture, where no rupture or repair has occurred participants have been censored at 21st November 2016 or date of death	
End point type	Primary
End point timeframe:	
Start date - 21st November 2016	

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: There was no statistical analyses for this end point

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed	342			
Units: Number of events	140			

Statistical analyses

No statistical analyses for this end point

Primary: AAA Repair

End point title	AAA Repair[2]
End point description:	
Time to event has been determined by the number of days between consent and repair, where no repair has occurred participants have been censored at 21st November or at date of death	
End point type	Primary
End point timeframe:	
Start date - 21st November 2016	

Notes:

[2] - 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: There was no statistical analyses for this primary end point

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Number of events	126			

Statistical analyses

No statistical analyses for this end point

Primary: AAA Rupture

End point title	AAA Rupture[3]

End point description:

Time to event has been determined by the number of days between consent and rupture, where no rupture has occurred participants have been censored at 21st November 2016 or date of death

End point type	Primary

End point timeframe:

Start date - 21st November 2016

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: There was no statistical analyses for this primary end point

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Number of events	17			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Date participant signs the consent form to last trial follow-up visit

Adverse event reporting additional description:

Trial nurses asked participants about AEs during follow-up visits and details of all events were recorded on the trial AE logs

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	All consented participants

Reporting group description:

All participants who have given consent for the trial are included in this group

Serious adverse events	All consented participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	163 / 342 (47.66%)		
number of deaths (all causes)	48		
number of deaths resulting from adverse events	33		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
any neoplasms benign, malignant and unspecified			
subjects affected / exposed	21 / 342 (6.14%)		
occurrences causally related to treatment / all	0 / 22		
deaths causally related to treatment / all	0 / 8		
Vascular disorders			
Any vascular disorder			
subjects affected / exposed	9 / 342 (2.63%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 2		
Surgical and medical procedures			
Any surgical and medical procedure			
subjects affected / exposed	20 / 342 (5.85%)		
occurrences causally related to treatment / all	0 / 20		
deaths causally related to treatment / all	0 / 0		
General disorders and administration			

site conditions			
Any general disorders and administration site conditions			
subjects affected / exposed	15 / 342 (4.39%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 8		
Reproductive system and breast disorders			
Any reproductive system and breast disorders			
subjects affected / exposed	3 / 342 (0.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Any respiratory, thoracic and mediastinal disorder			
subjects affected / exposed	4 / 342 (1.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Investigations			
Any investigations			
subjects affected / exposed	2 / 342 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
any injury, poisoning and procedural complications			
subjects affected / exposed	10 / 342 (2.92%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Any cardiac disorder			
subjects affected / exposed	16 / 342 (4.68%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 7		
Nervous system disorders			
Any nervous system disorder			

subjects affected / exposed	8 / 342 (2.34%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 2		
Gastrointestinal disorders			
Any gastrointestinal disorder			
subjects affected / exposed	11 / 342 (3.22%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Any hepatobiliary disorders			
subjects affected / exposed	1 / 342 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Any renal and urinary disorders			
subjects affected / exposed	5 / 342 (1.46%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Any musculoskeletal and connective tissue disorders			
subjects affected / exposed	5 / 342 (1.46%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Any infections and infestations			
subjects affected / exposed	32 / 342 (9.36%)		
occurrences causally related to treatment / all	0 / 38		
deaths causally related to treatment / all	0 / 5		
Metabolism and nutrition disorders			
Any metabolism and nutrition disorder			
subjects affected / exposed	1 / 342 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All consented participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	184 / 342 (53.80%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Any neoplasms benign, malignant and unspecified			
subjects affected / exposed	23 / 342 (6.73%)		
occurrences (all)	24		
Vascular disorders			
Any vascular disorder			
subjects affected / exposed	11 / 342 (3.22%)		
occurrences (all)	11		
Surgical and medical procedures			
Any surgical and medical procedure			
subjects affected / exposed	28 / 342 (8.19%)		
occurrences (all)	31		
General disorders and administration site conditions			
Any general disorder and administration site condition			
subjects affected / exposed	11 / 342 (3.22%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Any respiratory, thoracic and mediastinal disorder			
subjects affected / exposed	16 / 342 (4.68%)		
occurrences (all)	19		
Investigations			
Any investigation			
subjects affected / exposed	25 / 342 (7.31%)		
occurrences (all)	25		
Injury, poisoning and procedural complications			
Any injury, poisoning and procedural complication			
subjects affected / exposed	23 / 342 (6.73%)		
occurrences (all)	24		
Cardiac disorders			

Any cardiac disorders subjects affected / exposed occurrences (all)	20 / 342 (5.85%) 21		
Nervous system disorders Any nervous system disorder subjects affected / exposed occurrences (all)	13 / 342 (3.80%) 16		
Blood and lymphatic system disorders Any blood and lymphatic system disorder subjects affected / exposed occurrences (all)	1 / 342 (0.29%) 1		
Eye disorders Any eye disorder subjects affected / exposed occurrences (all)	1 / 342 (0.29%) 1		
Gastrointestinal disorders Any gastrointestinal disorders subjects affected / exposed occurrences (all)	27 / 342 (7.89%) 30		
Skin and subcutaneous tissue disorders Any skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	2 / 342 (0.58%) 2		
Renal and urinary disorders Any renal and urinary disorder subjects affected / exposed occurrences (all)	4 / 342 (1.17%) 4		
Endocrine disorders Any endocrine disorders subjects affected / exposed occurrences (all)	1 / 342 (0.29%) 1		
Musculoskeletal and connective tissue disorders Any musculoskeletal and connective tissue disorder subjects affected / exposed occurrences (all)	16 / 342 (4.68%) 17		
Infections and infestations			

Any infection and and infestation subjects affected / exposed occurrences (all)	53 / 342 (15.50%) 60		
Metabolism and nutrition disorders Any metabolism and nutrition disorder subjects affected / exposed occurrences (all)	3 / 342 (0.88%) 3		

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

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

NA

Notes: