Clinical trial results:
Randomised controlled trial comparing foam sclerotherapy, alone or in combination with endovenous laser therapy, with conventional surgery as a treatment for varicose veins

Summary

EudraCT number	2008-001069-26
Trial protocol	GB
Global end of trial date	29 November 2018

Results information

Result version number	v1 (current)
This version publication date	13 February 2019
First version publication date	13 February 2019

Trial information

Trial identification

Sponsor protocol code	06/45/02

Additional study identifiers

ISRCTN number	ISRCTN51995477
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Aberdeen
Sponsor organisation address	Foresterhill House Annex, Foresterhill, Aberdeen, United Kingdom, AB25 2ZD
Public contact	Julie Brittenden, University of Glasgow, 0141 2321795, Julie.Brittenden@glasgow.ac.uk
Scientific contact	Julie Brittenden, University of Glasgow, 0141 2321795, Julie.Brittenden@glasgow.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	29 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2018
Global end of trial reached?	Yes
Global end of trial date	29 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the clinical and cost-effectiveness of conventional surgery with two minimally invasive treatment modalities (a) foam sclerotherapy alone of main long or short saphenous trunk and non-trunk varicosities and (b) Endovenous laser ablation (EVLA) of main trunk including foam sclerotherapy of non-trunk varicosities, if required, performed under local anaesthetic in respect of quality of life for each intervention at 6 months (and ultimately through to 5 years) and cost-effectiveness as cost per quality adjusted life year (QALY) gained

Protection of trial subjects:

All trial subjects provided fully informed consent. Trial oversight by Sponsor, independent data monitoring and trial steering committees.

Background therapy:

Participants may have been on background therapy - this was not changed in the context of the trial

Evidence for comparator:

Surgery has been used in the treatment of varicose veins for many years. Ultrasound-guided foam sclerotherapy and endovenous laser ablation are widely used
alternatives to surgery for the treatment of varicose veins, but their comparative effectiveness and safety remain uncertain.

Actual start date of recruitment	03 November 2008
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: 785
Worldwide total number of subjects	785
EEA total number of subjects	785

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)	672
From 65 to 84 years	112
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Potentially eligible patients were provided with information about the trial; those providing fully informed consent were randomised. 8 hospitals randomised participants to all three treatment options; 3 hospitals randomised to surgery and foam sclerotherapy only.

Pre-assignment

Screening details:

Patients referred to one of 11 UK vascular surgery departments were screened for eligibility.

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:

None

Arms

Are arms mutually exclusive?	Yes
Arm title	Foam Sclerotherapy

Arm description:

Up to four treatments with foam sclerotherapy injected into the varicose vein(s)

Arm type	Experimental
Investigational medicinal product name	fibrovein
Investigational medicinal product code	C05BB04
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Other use

Dosage and administration details:

Foam was produced with the use of the Tessari technique at a ratio of 0.5ml of sodium tetradecyl sulphate to 1.5ml air, with a maximum of 12 ml of foam per session. 3% sodium tetradecyl sulphate was used for saphenous veins, 1% sodium tetradecyl sulphate was used for varicosities.

Arm title	Surgery

Arm description:

Conventional surgery for varicose veins

Arm type	surgical active comparator

No investigational medicinal product assigned in this arm

Arm title	Laser therapy

Arm description:

Endovenous laser ablation, with up to four sessions of foam sclerotherapy to residual varicose veins.

Arm type	Surgical active comparator

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Foam Sclerotherapy	Surgery	Laser therapy
Started	286	289	210
Completed	251	236	183
Not completed	35	53	27
Lost to follow-up	35	53	27

Baseline characteristics

Reporting groups	
Reporting group title	Foam Sclerotherapy
Reporting group description:	
Up to four treatments with foam sclerotherapy injected into the varicose vein(s)	
Reporting group title	Surgery
Reporting group description:	
Conventional surgery for varicose veins	
Reporting group title	Laser therapy
Reporting group description:	
Endovenous laser ablation, with up to four sessions of foam sclerotherapy to residual varicose veins.	

Reporting group values	Foam Sclerotherapy	Surgery	Laser therapy
Number of subjects	286	289	210
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	250	253	169
From 65-84 years	36	35	41
85 years and over	0	1	0
Age continuous			
Age (years)			
Units: years			
arithmetic mean	49.0	49.2	49.7
standard deviation	± 13.3	± 13.7	± 14.4
Gender categorical Units: Subjects			
Female	162	163	120
Male	124	126	90

Reporting group values	Total		
Number of subjects	785		
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)	672		
From 65-84 years	112		
85 years and over	1		
Age continuous			
Age (years)			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	445		
Male	340		

End points

End points reporting groups

Reporting group title	Foam Sclerotherapy
Reporting group description: Up to four treatments with foam sclerotherapy injected into the varicose vein(s)	
Reporting group title	Surgery
Reporting group description: Conventional surgery for varicose veins	
Reporting group title	Laser therapy
Reporting group description: Endovenous laser ablation, with up to four sessions of foam sclerotherapy to residual varicose veins.	
Subject analysis set title	6 month intention to treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants attending for 6 month follow-up	

Primary: Aberdeen Varicose Vein Questionnaire

End point title	Aberdeen Varicose Vein Questionnaire
End point description:	
End point type	Primary
End point timeframe: 6 months	

End point values	Foam Sclerotherapy	Surgery	Laser therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	238	214	175	
Units: points				
arithmetic mean (standard deviation)	9.1 (± 7.9)	7.8 (± 7.5)	7.9 (± 8.4)	

Statistical analyses

Statistical analysis title	surgery vs foam
Comparison groups	Surgery v Foam Sclerotherapy
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-0.5
Variability estimate	Standard error of the mean

Statistical analysis title	surgery vs laser
Comparison groups	Surgery v Laser therapy
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0.9
Variability estimate	Standard error of the mean

Statistical analysis title	laser vs foam
Comparison groups	Laser therapy v Foam Sclerotherapy
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.4
Variability estimate	Standard error of the mean

Primary: EQ-5D	
End point title	EQ-5D
End point description:	

End point type	Primary
End point timeframe:	
6 months	

End point values	Foam Sclerotherapy	Surgery	Laser therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	238	214	175	
Units: points				
arithmetic mean (standard deviation)	0.895 (± 0.174)	0.881 (± 0.202)	0.903 (± 0.171)	

Statistical analyses

Statistical analysis title	surgery vs foam
Comparison groups	Foam Sclerotherapy v Surgery
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.025
upper limit	0.035
Variability estimate	Standard error of the mean

Statistical analysis title	surgery vs laser
Comparison groups	Surgery v Laser therapy
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.051
upper limit	0.021
Variability estimate	Standard error of the mean

Statistical analysis title	laser vs foam
Comparison groups	Laser therapy v Foam Sclerotherapy

Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.025
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.059
Variability estimate	Standard error of the mean

Primary: SF-36 Physical component

End point title	SF-36 Physical component
End point description:	
End point type	Primary
End point timeframe:	
6 months	

End point values	Foam Sclerotherapy	Surgery	Laser therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	238	214	175	
Units: points				
arithmetic mean (standard deviation)	52.3 (± 8.5)	52.4 (± 8.9)	52.6 (± 7.3)	

Statistical analyses

Statistical analysis title	surgery vs foam
Comparison groups	Surgery v Foam Sclerotherapy
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.3
Variability estimate	Standard error of the mean

Statistical analysis title	surgery vs laser
Comparison groups	Surgery v Laser therapy
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.6
Variability estimate	Standard error of the mean

Statistical analysis title	laser vs foam
Comparison groups	Laser therapy v Foam Sclerotherapy
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	2.1
Variability estimate	Standard error of the mean

Primary: SF-36 Mental component	
End point title	SF-36 Mental component
End point description:	

End point type	Primary
End point timeframe:	
6 months	

End point values	Foam Sclerotherapy	Surgery	Laser therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	238	214	175	
Units: points				
arithmetic mean (standard deviation)	52.2 (± 9.1)	52.1 (± 8.6)	53.5 (± 7.7)	

Statistical analyses

Statistical analysis title	surgery vs foam
Comparison groups	Surgery v Foam Sclerotherapy
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.6
Variability estimate	Standard error of the mean

Statistical analysis title	surgery vs laser
Comparison groups	Surgery v Laser therapy
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	0.2
Variability estimate	Standard error of the mean

Statistical analysis title	laser vs foam
Comparison groups	Laser therapy v Foam Sclerotherapy

Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.1
Variability estimate	Standard error of the mean

Secondary: Success of ablation of the great saphenous vein

End point title	Success of ablation of the great saphenous vein
End point description:	
End point type	Secondary
End point timeframe:	
6 months	

End point values	Foam Sclerotherapy	Surgery	Laser therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182	173	141	
Units: subjects				
Complete success	79	135	116	
Partial success without reflux	35	4	13	
Partial success with reflux	9	20	3	
Failure	59	14	9	

Statistical analyses

Statistical analysis title	surgery vs foam
Comparison groups	Surgery v Foam Sclerotherapy
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	7.9

Variability estimate	Standard error of the mean

Statistical analysis title	surgery vs laser
Comparison groups	Surgery v Laser therapy
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.5
Variability estimate	Standard error of the mean

Statistical analysis title	laser vs foam
Comparison groups	Laser therapy v Foam Sclerotherapy
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	8.5
Variability estimate	Standard error of the mean

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Foam Sclerotherapy
Reporting group description: Up to four treatments with foam sclerotherapy injected into the varicose vein(s)	
Reporting group title	Surgery
Reporting group description: Conventional surgery for varicose veins	
Reporting group title	Laser therapy
Reporting group description: Endovenous laser ablation, with up to four sessions of foam sclerotherapy to residual varicose veins.	

Serious adverse events	Foam Sclerotherapy	Surgery	Laser therapy
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 286 (3.85%)	10 / 289 (3.46%)	7 / 210 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
myeloma			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	0 / 210 (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
breast cancer			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	0 / 210 (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
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 286 (0.00%)	0 / 289 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
postoperative haematoma			
subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peroneal nerve injury			
subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 286 (0.00%)	0 / 289 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Site specific injuries NEC			
subjects affected / exposed	0 / 286 (0.00%)	0 / 289 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 286 (0.35%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 286 (1.05%)	0 / 289 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
palpitation			
subjects affected / exposed	0 / 286 (0.00%)	0 / 289 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			

Surgery			
subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Involuntary commitment			
subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
migraine			
subjects affected / exposed	0 / 286 (0.00%)	0 / 289 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	0 / 210 (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
Headache			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	0 / 210 (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
stroke			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	0 / 210 (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
Gastrointestinal disorders			
ANAL POLYP			
subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
BREAST ENLARGEMENT			

subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 286 (0.00%)	1 / 289 (0.35%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
urinary retention			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	0 / 210 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 286 (0.35%)	0 / 289 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Post procedural infection			
subjects affected / exposed	0 / 286 (0.00%)	2 / 289 (0.69%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Foam Sclerotherapy	Surgery	Laser therapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 286 (50.35%)	109 / 289 (37.72%)	89 / 210 (42.38%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	38 / 286 (13.29%)	40 / 289 (13.84%)	25 / 210 (11.90%)
occurrences (all)	38	40	25
Lumpiness			

subjects affected / exposed	67 / 286 (23.43%)	17 / 289 (5.88%)	25 / 210 (11.90%)
occurrences (all)	67	17	25
Vascular disorders			
development of thread veins			
subjects affected / exposed	34 / 286 (11.89%)	26 / 289 (9.00%)	24 / 210 (11.43%)
occurrences (all)	34	26	24
Nervous system disorders			
NUMBNESS			
subjects affected / exposed	10 / 286 (3.50%)	37 / 289 (12.80%)	17 / 210 (8.10%)
occurrences (all)	10	37	17
Skin and subcutaneous tissue disorders			
Skin loss or ulceration			
subjects affected / exposed	2 / 286 (0.70%)	0 / 289 (0.00%)	1 / 210 (0.48%)
occurrences (all)	2	0	1
Skin staining			
subjects affected / exposed	92 / 286 (32.17%)	24 / 289 (8.30%)	32 / 210 (15.24%)
occurrences (all)	82	24	32

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 September 2008	Section 4.2 – deleted 'and are suitable for day case treatment' from the inclusion criteria. Section 4.8.3 – added expected serious adverse events related to laser and surgery and additional expected serious adverse events related to foam.
06 February 2009	Section 4.1 – revision of detail re fibrovein administration and addition of info re labelling and storage; removal of specific type of laser. Section 4.2 – clarification re HRT. Section 4.3 – addition of detail re clinic log, postal information leaflet, consent by post. Section 4.4 – clarification of randomisation and post-randomisation processes. Section 4.7 – addition of VAS to assess pain during treatment; timing of BRQ.
17 June 2009	Section 4 – revision to add additional (unnamed) sites. Section 7.3 – removal of sentence relating to joint sponsorship.
23 October 2009	Section 4.8.3 - inclusion of TIA as an expected adverse reaction following foam sclerotherapy.
22 February 2010	Section 4.8.1 – revision of definition of SAE: inclusion of category 'an important medical event that may not be immediately life threatening or result in death, but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition'.
08 October 2010	Section 4.1 – rewording of paragraph detailing the storage and temperature monitoring of Fibrovein. Section 6.4 – revised recruitment rates. Section 4 – rewording of paragraph on trial design.
25 May 2011	Section 4.1 – rewording of paragraph detailing Fibrovein labelling; removal of obligation to label FV
08 November 2011	Addition of migraines 'which are frequent…or…severe enough to require hospitalisation' as an exclusion criteria. Addition of migraine as an expected AE following foam sclerotherapy.

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.

There was no blinding.
Comparison did not include radio-frequency ablation.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25251616

http://www.ncbi.nlm.nih.gov/pubmed/25858333

http://www.ncbi.nlm.nih.gov/pubmed/25274220

http://www.ncbi.nlm.nih.gov/pubmed/26805720