



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 (\pm 7.9) | 7.8 (\pm 7.5) | 7.9 (\pm 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 occurrences (all) | 67 / 286 (23.43%) 67 | 17 / 289 (5.88%) 17 | 25 / 210 (11.90%) 25 |
| Vascular disorders development of thread veins subjects affected / exposed occurrences (all) | 34 / 286 (11.89%) 34 | 26 / 289 (9.00%) 26 | 24 / 210 (11.43%) 24 |
| Nervous system disorders NUMBNESS subjects affected / exposed occurrences (all) | 10 / 286 (3.50%) 10 | 37 / 289 (12.80%) 37 | 17 / 210 (8.10%) 17 |
| Skin and subcutaneous tissue disorders Skin loss or ulceration subjects affected / exposed occurrences (all) | 2 / 286 (0.70%) 2 | 0 / 289 (0.00%) 0 | 1 / 210 (0.48%) 1 |
| Skin staining subjects affected / exposed occurrences (all) | 92 / 286 (32.17%) 82 | 24 / 289 (8.30%) 24 | 32 / 210 (15.24%) 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 fibro vein 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 Fibro vein. Section 6.4 – revised recruitment rates. Section 4 – rewording of paragraph on trial design. |
| 25 May 2011 | Section 4.1 – rewording of paragraph detailing Fibro vein 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>