The INTERVENE trial: A novel percutaneous device to reconstruct the valves within the femoral veins in patients with DVI

Ramon L. Varcoe MBBS, MS, FRACS, PhD, MMed (ClinEpi)
Prince of Wales Hospital and University of New South Wales
Sydney, Australia
Disclosures

Consultant to:
- Medtronic
- Abbott Vascular
- BD Bard
- Intervene
- Surmodics
- Philips Healthcare
- Nectero Medical
- Alucent Biomedical

Shareholder:
- W.L. Gore
- R3 Vascular
- EBR Systems
- Provisio Medical, inc
- Vesteck Inc
Deep Venous Reflux (DVR) is Linked to Severe Disease

The Bonn Vein Study shows high prevalence of DVR in the advanced, severe CVI population; those with skin changes and ulceration

DVR is Prevalent in Non-Healing & Recurring VLUs

Freedom from Ulcer Recurrence after endovenous laser ablation (EVLA) Patients with only Superficial reflux vs concomitant Deep and Superficial reflux

Patients with concomitant DVR had significantly increased risk of ulcer recurrence compared with those with superficial reflux alone.

Marston et al. J. Vasc Surg. 2017.02.007
Clinical Results

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<th>Surgeon</th>
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ᵃ: 3 Recurrent Ulcers in Maleti’s group
ᵇ: 2 Recurrences of symptoms in Hoshino’s group

2. Hoshino et al, EVF 2016 abstract
Surgical Predicate – The Maleti Neovalve

Neovalve construction in deep venous incompetence

Marzia Lugli, MD,* Sara Guerzoni, BS,* Mariano Garofalo, MD,* Gianluca Smedile, MD, b and Oscar Maleti, MD,* Modena and Rome, Italy

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Endovenous Valve Formation (EVF)

- Cath-based non-implant Tx for DVR
- 16Fr Retrograde CFV Access
- IVUS and Fluoro guided
- Multiple Valves per Procedure
- Monocuspid and bicuspid capable
BlueLeaf EndoVenous Valve Formation
(Cadaveric Monocuspid valve shown)

Edited for speed
INFINITE-IOUS STUDY: Results Published in JVS-VL

- BlueLeaf EVF (Gen 2) Safety & Feasibility of n=14 patients, f/u to 3 yr
- 5.6pt Mean VCSS improvement
- Demonstrated viability & safety of EVF (Endovenous Valve Formation)
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Optimizing BlueLeaf’s Dissector Geometry for Larger Coapting Valves

- Canted & wider Dissector arms tangential orientation improved dissection
- Increased valve size capability
- Additional, larger size needed for larger veins and co-aptation
**BlueLeaf Clinical Research Program Update**

**41 Cases To Date**

**INFINITE – US**
- Sites: 5
- Enrollment: 15
- Device: Gen 3A, 3B, 3B+, 3C+
- # Valves: Max 2 mono or bicusp
- Bicuspid allowed: ✓
- DUS & APG metrics
- Wound Care Centers for Ulcer patients
- CEAP 5/6

**INFINITE – RoG**
- Sites: 2
- Enrollment: 8
- Device: Gen 3B+
- # Valves: Unlimited
- Bicuspid allowed: ✓
- Flexibility for procedure; Bicuspid, local drug delivery
- Visiting docs can scrub in
- CEAP 4-6
- Importance of Post-Op care
- DUS valve imaging

**INFINITE – OUS**
- Sites: 5 (AUS:2, NZ:2, CAN:1)
- Enrollment: 18
- Device: Gen 2, 3D+
- # Valves: Unlimited
- Bicuspid allowed: ✓
- FIM viability, safety, rapid technique improvement, room prep, staff training, proctoring
- Established limitations of Gen 2
- CEAP 4-6
- Access & closure, optimal IVUS
Study Title: BlueLeaf Global Clinical Research Program

Study Device: BlueLeaf® Endovenous Valve Formation System (BlueLeaf System) – Gen 2 >> 3

Sites: 12 (5 in US; 2 in Tbilisi, Georgia; 2 in AUS; 2 in NZ; 1 in CAN)

Key Inclusion / Exclusion Criteria:
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<tr>
<td>Mean ± SD</td>
<td>1.8 ± 0.7</td>
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<tr>
<td>(Min, Max)</td>
<td>(0, 3)</td>
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<td>Mean ± SD</td>
<td>03:01 ± 00:45</td>
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<tr>
<td>(Min, Max)</td>
<td>(01:42, 04:36)</td>
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<td>Device in Body Time (hh:mm)</td>
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Major Adverse Events:
- 2 – Failed venotomy closures requiring reintervention
- 1 – Asymptomatic DVT, seen by DUS at discharge and recanalized by 30 days
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### Valve Type Distribution
- **Monocuspid**: 56%
- **Bicuspid**: 17%
- **Single Monocuspid, Single Bicuspid**: 15%
- **Single Monocuspid, Double Bicuspid**: 7%
- **No Valve**: 5%
## Valve Statistics and Safety Outcomes

### Major Adverse Events:
- 2 – Failed venotomy closures requiring reintervention
- 1 – Asymptomatic DVT, seen by DUS at discharge and recanalized by 30 days

<table>
<thead>
<tr>
<th>Category</th>
<th>Result</th>
<th>(n = 41 subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural Success</td>
<td>39/41 (95.1%)</td>
<td></td>
</tr>
<tr>
<td>Number of valves (mono or bi)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (Min, Max)</td>
<td>1.8 ± 0.7 0, 3</td>
<td></td>
</tr>
<tr>
<td>Procedure Time (hh:mm)</td>
<td>03:01 ± 00:45 (01:42, 04:36)</td>
<td></td>
</tr>
<tr>
<td>Device in Body Time (hh:mm)</td>
<td>01:31 ± 00:31 (00:44, 02:48)</td>
<td></td>
</tr>
</tbody>
</table>

### Valve Type Distribution
- Monocuspid: 56%
- Single Monocuspid, Single Bicuspid: 15%
- Single Monocuspid, Double Bicuspid: 7%
- Bicuspid: 17%
Venous Clinical Severity Score (VCSS)

VCSS - Global

Pre-procedure 30-Day 12-Week 210-Day 365-Day

<table>
<thead>
<tr>
<th></th>
<th>Pre-procedure</th>
<th>30-Day</th>
<th>12-Week</th>
<th>210-Day</th>
<th>365-Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n = 41</td>
<td>n = 41</td>
<td>n = 40</td>
<td>n = 37</td>
<td>n = 32</td>
</tr>
<tr>
<td>Mean US</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Mean RoG</td>
<td></td>
<td></td>
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<tr>
<td>Mean OUS</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

-2.6 -3.5 -4.1 -5.5

VCSS
Do More Valves (and more Bicuspid) Improve Results? The Varcoe Index

<table>
<thead>
<tr>
<th>Group Name</th>
<th>Category</th>
<th>Scoring Method</th>
<th>Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI - 0</td>
<td>No valve created</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>VI - 1</td>
<td>Monocusp (x1)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VI - 2</td>
<td>Monocusp (x2) or Bicuspid (x1)</td>
<td>1+1 or 2</td>
<td>2</td>
</tr>
<tr>
<td>VI - 3</td>
<td>Monocusp (x3) or Monocusp (x1) + Bicuspid (x1)</td>
<td>1+1+1 or 1+2</td>
<td>3</td>
</tr>
<tr>
<td>VI - 4</td>
<td>Bicuspid (x2)</td>
<td>2+2</td>
<td>4</td>
</tr>
<tr>
<td>VI - 5</td>
<td>Bicuspid (x2) + Monocusp (x1)</td>
<td>2+2+1</td>
<td>5</td>
</tr>
</tbody>
</table>

**Scoring Methodology**

0 = No valves  
1 = Monocusp  
2 = Bicuspid
Optimization continues w/Device Design & Procedural Technique(s)

Gen I, II, III demonstrated repeatability and safety (low DVT), Gen III + new Clocking technique for improved valve geometry and competence

Rotating ‘Clock Position during Dissection & Mouth Cut Steps

Gen IV
Prince of Wales, Sydney Case (11/11/22) Completion
Conclusions from INFINITE Global Study

- Deep venous reflux is a morbid condition with few treatment options

- The Blueleaf is able to safely and consistently create a series of fully autogenous neovalves percutaneously

- Both monocuspid and bicuspid configurations

- Consistent reductions observed in rVCSS

- Gen IV Design & techniques underway to improve valve function (focused on coaptation/competency, large veins)

With team of Prof Ramon Varcoe & Dr. Gigi Bregadze, Tbilisi Heart & Vascular Clinic, Tbilisi, RoG
The INTERVENE trial: A novel percutaneous device to reconstruct the valves within the femoral veins in patients with DVI

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