VIRTUS trial update

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Disclosures

- For the 12 months preceding this CME activity, I disclose the following types of financial relationships:

  • Consulted for:
    - Medtronic, Microvention/Terumo, LAS Inc., Penumbra, Reflow
    - Medical, Soundbite Medical, Veniti, Walk Vascular

  • Research, clinical trial, or study funds received from:
    - Boston Scientific Inc., Bard Periph Vasc., Mercator, Spectranetics,
    - National Institutes of Health, Veniti

VICI VENOUS STENT

- Designed for:
  • Strength: High crush resistance
  • Flexibility: Multi-directional
  • Crush Resistance (end-to-end): Lumens shape
  • Coverage: No gaps, closed-cell
  • Deployment: Predictable placement

- Self-expanding Nickel-Titanium (Nitinol)
- 12, 14, and 16 mm diameter
- 60, 90, and 120 mm length
- Two delivery systems for controlled stent placement centrally or peripherally

VICI VENOUS STENTVICI VERTO VENOUS STENT

- Delivery Systems:
  • Coaxial design
  • Over-the-wire system compatible with:
    - 0.035" guide wires
    - VICI 9F introducer sheath
    - VERTO 10F introducer sheath
  • Femoral, popliteal, or jugular approach

VIRTUS Trial Design

- Objective: Assess safety & effectiveness in achieving patency of target venous lesion through 12 months post stent placement, in patients with obstruction of the iliofemoral venous outflow tract

- Principal Investigators:
  - Dr. William Marston
  - Dr. Mahmood Razavi

- Study Design: Prospective, multicenter, single arm non-randomized

- Patients: Feasibility: N=30 (9 sites)
Pivotal: N=170 (22 sites)
USA and Europe

- Endpoints:
  • Safety: MAEs @ 30 days
  • Effectiveness: Primary Patency @ 12 Months

- Core labs:
  - Venography: Syntactx
  - IVUS: St. Lukes
  - X-Ray: Syntactx

VIRTUS Trial Design

Key Inclusion Criteria:

- Unilateral, clinically significant, chronic non-malignant obstruction of the common femoral vein, external iliac vein, common iliac vein, or any combination thereof
- ≥50% reduction in target vessel lumen diameter (venogram)
- Clinically significant venous obstruction defined as: CEAP "C" ≥3 or VCSS Pain ≥2

Imaging Schedule

- Pre-stent
- Post-stent
- 12 Months
- Venography
- SYMPTOMS
- PRIMARY PATENCY
- MAEs
- 30 days
CEAP Classification of Venous Disease

<table>
<thead>
<tr>
<th>C: Clinical</th>
<th>D: Biomechanical</th>
<th>A: Anatomical</th>
<th>P: Pathophysiologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No venous disease</td>
<td>0: Congestion</td>
<td>0: Superficial veins</td>
<td>0: Reflux</td>
</tr>
<tr>
<td>1: Telangiectases</td>
<td>1: Primary (leg)</td>
<td>1: Perforator veins</td>
<td>No Obstruction</td>
</tr>
<tr>
<td>2: Varicosities</td>
<td>2: Secondary (perinephric)</td>
<td>2: Deep veins</td>
<td>Krukenberg and Obstruction</td>
</tr>
<tr>
<td>3: Edema</td>
<td>3: Lipodermatosclerosis and atrophie blanche</td>
<td>3: No venous pathophysiology siadable</td>
<td></td>
</tr>
<tr>
<td>4: Lipodermatosclerosis and atrophie blanche</td>
<td>4: Telangiectasies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5: Active ulcer</td>
<td>5: Edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6: Healed ulcer</td>
<td>6: Telangiectasies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7: Telangiectasies</td>
<td>7: Edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8: No venous disease</td>
<td>8: Telangiectasies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9: Ulcer presence</td>
<td>9: Edema</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Endpoint

Primary Safety

Effectiveness

Primary

A: asymptomatic

C6: Active ulcer

C5: Healed ulcer

C4a: Pigmentation and atrophie blanche

C3: Edema

C2: Telangiectasies

C1: Telangiectasies

C0: No venous disease

Target Limb VCSS Leg Pain

CEAP "C" Assessment

Obstruction present in:

Clinical Assessment N=170

Table: Observed Proportion of Subjects by Obstruction Category

<table>
<thead>
<tr>
<th>Obstruction Category</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>10.3%</td>
</tr>
<tr>
<td>Mild</td>
<td>34.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td>37.0%</td>
</tr>
<tr>
<td>Severe</td>
<td>18.7%</td>
</tr>
</tbody>
</table>

Baseline Patient Characteristics

Venous Stent Trials

PTS Severity

<table>
<thead>
<tr>
<th>PTS Present</th>
<th>NSD Moderate</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Villalta</td>
<td>5-9</td>
<td>10-14</td>
</tr>
<tr>
<td>&lt;5 or ulcer</td>
<td>5-9</td>
<td>10-14</td>
</tr>
<tr>
<td>&gt;15 or ulcer</td>
<td>5-9</td>
<td>10-14</td>
</tr>
</tbody>
</table>

VILLAS PTS Score

- Patient Assessment
  - Pain
  - Edema
  - Telangiectasies
  - Hyperpigmentation
  - Pruritus

- Clinician Assessment
  - Paresthesias
  - Leg heaviness
  - Paresthesias
  - Leg heaviness

- Ulcer presence
  - No ulcer
  - Active ulcer
  - Healed ulcer
  - Ulcer presence

Venous Stent Trials

<table>
<thead>
<tr>
<th>Study/Phase</th>
<th>Stent Type</th>
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<tbody>
<tr>
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<td>VICI (Boston)</td>
<td>VILLAS</td>
<td>Zilver (Cook)</td>
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VENUS, a multicenter, single-arm study, assessed the safety and efficacy of the VENUS-1V PALE (Bard) stent in the treatment of a symptomatic iliofemoral venous disease. The study enrolled patients with symptomatic iliofemoral venous obstruction at 31 centers in Europe and was led by Dr. Thurner. The study was sponsored by Bard, an American company. The study enrolled 200 patients with symptomatic iliofemoral venous obstruction and was sponsored by Bard. The study enrolled 200 patients with symptomatic iliofemoral venous obstruction and was sponsored by Bard. The study enrolled 200 patients with symptomatic iliofemoral venous obstruction and was sponsored by Bard. The study enrolled 200 patients with symptomatic iliofemoral venous obstruction and was sponsored by Bard. The study enrolled 200 patients with symptomatic iliofemoral venous obstruction and was sponsored by Bard.
Results in Lower Extremities

- Non-thrombotic (NT) 96% [90-99%]
- Acute thrombotic (AT) 86% [80-90%]
- Chronic post thrombotic (CPT) 79% [70-80%]

Conclusions

- Venous anatomy and disease require dedicated venous stents
- Venous stent studies have important differences in inclusion criteria and endpoint measures
- VIRTUS feasibility data (n=30) demonstrate high 1-year patency rate and symptom improvement
- VIRTUS pivotal cohort (n=170) includes a high proportion of patients with PTS, awaiting 12-month primary endpoint analysis