VENOVO Venous Stent Trial: 12-Month Update

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University of Arizona Health Sciences
Tucson, Arizona

Disclosures
• Research/Research Grants, Clinical Trial Support
  – W. L. Gore
  – Cook Medical
• Consulting Fees/Honoraria
  – W. L. Gore
  – Cook Medical
  – Novate Medical
• Officer, Director, Board Member or other Fiduciary Role
  – VIVA Physicians Group
• Speaker, Other
  – None

VERNACULAR Study Objective
Assess the performance of the VENOVO Venous Stent for the treatment of iliac & femoral vein occlusive disease, including acute or chronic deep vein thrombosis (DVT) and/or May-Thurner Syndrome

Principal Investigator: Michael Dake
Co-Principal Investigator (Europe): Gerard O’Sullivan

VERNACULAR Study Overview
• Design: Prospective, Multicenter, Non-Randomized, Single-Arm
  – Patient Population: 170 patients
  – 22 International Sites: USA, Europe, and Australia
• Independent Analysis:
  – Venographic & radiographic assessment: Yale Core Lab
  – Duplex Ultrasound (DUS) evaluation: VasCore
  – Clinical Events Committee (CEC): adjudicated serious adverse events
  – Data Safety Monitoring Board: assessed overall patient safety
• Follow Up:
  – 12-month data presented today
  – Ongoing follow up through 3 years

Study Device: VENOVO® Venous Stent
• Self-expanding nitinol stent designed for veins
• 3 mm flared ends designed for vein wall apposition
• 8 radiopaque tantalum markers (3 on each end)
• Tri-axial, 0.035” over-the-wire delivery system

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Stent Sizes

<table>
<thead>
<tr>
<th>Stent Diameter</th>
<th>Stent Length (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mm</td>
<td>40 mm</td>
</tr>
<tr>
<td>12 mm</td>
<td>40 mm</td>
</tr>
<tr>
<td>14 mm</td>
<td>60 mm</td>
</tr>
<tr>
<td>16 mm</td>
<td>80 mm</td>
</tr>
<tr>
<td>18 mm</td>
<td>100 mm</td>
</tr>
<tr>
<td>20 mm</td>
<td>120 mm</td>
</tr>
<tr>
<td>5F</td>
<td>140 mm</td>
</tr>
<tr>
<td>7F</td>
<td>160 mm</td>
</tr>
</tbody>
</table>

Key Inclusion Criteria
• Symptomatic venous outflow obstruction in the iliac & femoral veins ≥ 50% (contrast venography)
• CEAP “C” (clinical score)1 ≥ 3 or VCSS (pain score)2 ≥ 2
• RV/D: 7 mm - 19 mm (visual estimate)

1 Clinical Score from the Clinical-Etiology-Anatomy-Pathophysiology (CEAP) Classification
2 Pain Score from the Venous Clinical Severity Score (VCSS)

VENOVO is a registered trademark of C. R. Bard, a wholly owned subsidiary of Becton, Dickinson and Company.
Key Exclusion Criteria

- Malignant obstruction
- Contralateral disease in the iliac & femoral veins
- Venous obstruction extending into the inferior vena cava or below the level of the lesser trochanter
- Prior stent placement at the site of the target lesion
- RVD < 7 mm or > 19 mm
- On dialysis or serum creatinine ≥ 2.5 mg/dl

Endpoints

- **Primary Efficacy:**
  - Freedom from target vessel revascularization (TVR) and thrombotic occlusion and stenosis > 50% measured by DUS (VascCore DUS Core Lab)
- **Primary Safety:**
  - Freedom from MAEs (30-days):
    - TVR
    - Device and/or procedure-related death
    - Target limb major amputation
    - Clinically relevant pulmonary embolism
    - Vascular injury requiring intervention
    - Embolization and/or imigration of stent
    - Device- and/or procedure-related acute DVT
- **Hypothesis-Tested Secondary Endpoints:**
  - VCSS Pain Score & Chronic Venous Insufficiency Questionnaire (CIVIQ-20):
    - Mean difference between baseline & 12 months

Primary Efficacy Endpoint (12 Months)

<table>
<thead>
<tr>
<th>ITT Population</th>
<th>PTS (N=93)</th>
<th>NIVL (N=77)</th>
<th>Total (N=170)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Patency, % (90% CI)</td>
<td>81.3% (72.4%, 88.7%)</td>
<td>96.9% (90.6%, 99.5%)</td>
<td>88.3% (82.4%, 94.2%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Procedural Data

<table>
<thead>
<tr>
<th>ITT</th>
<th>PTS (N=93)</th>
<th>NIVL (N=77)</th>
<th>Total (N=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Procedure Time, min ± SD</td>
<td>64.7 ± 32.9</td>
<td>48.8 ± 18.0</td>
<td>57.5 ± 28.2</td>
</tr>
<tr>
<td>Number of Stents Implant</td>
<td>134</td>
<td>85</td>
<td>219</td>
</tr>
<tr>
<td>Mean Stented Length, mm ± SD</td>
<td>109.2 ± 49.8</td>
<td>86.0 ± 45.2</td>
<td>100.6 ± 49.1</td>
</tr>
<tr>
<td>Final % Diameter Stenosis, % (pH)</td>
<td>16.2 ± 6.6</td>
<td>12.4 ± 5.9</td>
<td>14.2 ± 6.3</td>
</tr>
</tbody>
</table>

Patient Demographics

<table>
<thead>
<tr>
<th>ITT Population</th>
<th>PTS (N=93)</th>
<th>NIVL (N=77)</th>
<th>Total (N=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age, years ± SD</td>
<td>49.8 ± 15.0</td>
<td>55.0 ± 15.4</td>
<td>52.1 ± 15.3</td>
</tr>
<tr>
<td>Male/Female, %/%</td>
<td>45.2/54.8</td>
<td>27.3/72.7</td>
<td>37.2/62.9</td>
</tr>
<tr>
<td>Mean BMI, kg/m² ± SD</td>
<td>28.6 ± 6.4</td>
<td>28.8 ± 7.0</td>
<td>28.8 ± 7.0</td>
</tr>
<tr>
<td>Varicosis, % (n)</td>
<td>76.3 (71)</td>
<td>80.5 (62)</td>
<td>78.2 (133)</td>
</tr>
<tr>
<td>May-Thurner Syndrome, % (n)</td>
<td>37.6 (35)</td>
<td>87.0 (67)</td>
<td>60.0 (102)</td>
</tr>
<tr>
<td>Smoker (Current &amp; Former), % (n)</td>
<td>30.1 (28)</td>
<td>32.4 (28)</td>
<td>31.5 (22)</td>
</tr>
<tr>
<td>Hypertension, % (n)</td>
<td>29.0 (27)</td>
<td>36.4 (28)</td>
<td>32.4 (55)</td>
</tr>
<tr>
<td>Dyslipidemia, % (n)</td>
<td>21.5 (19)</td>
<td>35.1 (27)</td>
<td>27.6 (47)</td>
</tr>
<tr>
<td>Diabetes (Type 2), % (n)</td>
<td>5.4 (5)</td>
<td>16.9 (13)</td>
<td>10.6 (18)</td>
</tr>
<tr>
<td>Peripheral Artery Disease, % (n)</td>
<td>6.5 (6)</td>
<td>15.6 (12)</td>
<td>9.5 (16)</td>
</tr>
</tbody>
</table>

Lesion Characteristics

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<thead>
<tr>
<th>ITT</th>
<th>PTS (N=93)</th>
<th>NIVL (N=77)</th>
<th>Total (N=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Location, %</td>
<td>92.1</td>
<td>97.3</td>
<td>94.5</td>
</tr>
<tr>
<td>Lesion Morphology, % (n)</td>
<td>58.4</td>
<td>18.9</td>
<td>40.5</td>
</tr>
<tr>
<td>Thrombus Present, % (n/N)</td>
<td>14.8 (13/88)</td>
<td>1.4 (1/74)</td>
<td>8.6 (14/162)</td>
</tr>
<tr>
<td>No Blood Flow (Occluded), % (n/N)</td>
<td>38.6 (34/88)</td>
<td>4.1 (1/74)</td>
<td>22.8 (37/162)</td>
</tr>
<tr>
<td>% Diameter Stenosis, mean ± SD</td>
<td>81.0 ± 18.4</td>
<td>69.3 ± 12.6</td>
<td>75.7 ± 17.0</td>
</tr>
</tbody>
</table>
Freedom from Loss of Primary Patency

**Kaplan-Meier Sensitivity Analysis**

Time-to-event survival analysis: 395 days is the end of the 12-month follow-up interval

<table>
<thead>
<tr>
<th>Time (Days)</th>
<th>Survival Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>88.9% (83.9%, 92.4%)</td>
</tr>
</tbody>
</table>

Primary Safety Endpoint

**Freedom from MAEs (30 Days)**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Freedom from MAEs, % (90% CI)</th>
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<tbody>
<tr>
<td>ITT Population</td>
<td>N=93</td>
<td>88.2% (83.16%, 92.4%)</td>
</tr>
<tr>
<td>PTS N=45</td>
<td></td>
<td>100% (77/77)</td>
</tr>
<tr>
<td>NIVL N=77</td>
<td></td>
<td>93.5% (159/170)</td>
</tr>
<tr>
<td>Total N=170</td>
<td></td>
<td>89.5% (86.3%, 92.6%)</td>
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*Freedom from MAEs with VENOVO was better than a literature-derived performance goal (89%)*

Time-to-event survival analysis - 395 days is the end of the 12-month follow-up interval

Primary Endpoint:

**Freedom from MAEs (30 Days)**

Freedom from MAEs with VENOVO was better than a literature-derived performance goal (89%).

Primary Safety Endpoint:

**Freedom from MAEs (30 Days)**

Freedom from MAEs with VENOVO was better than a literature-derived performance goal (89%).

**ITT Population**

N=93

Freedom from MAEs, % (90% CI)

88.2% (83.16%, 92.4%)

**PTS N=45**

100% (77/77)

**NIVL N=77**

93.5% (159/170)

**Total N=170**

89.5% (86.3%, 92.6%)

P-value: 0.03

Secondary Endpoint: VCSS Pain Score

**Mean Improvement from Baseline**

-1.7 (95% CI: -1.8, -1.5)

(p = 0.001)

Secondary Endpoint: CIVIQ-20 Score

**Mean Improvement from Baseline**

-15.7 (95% CI: -18.4, -13.0)

(p < 0.0001)

Secondary Observations (12 Months)

<table>
<thead>
<tr>
<th>Group</th>
<th>Freedom from TLR &amp; TVR, % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT N=93</td>
<td>87.6 (78/89)</td>
</tr>
<tr>
<td>PTS N=45</td>
<td>98.6 (73/74)</td>
</tr>
<tr>
<td>NIVL N=77</td>
<td>92.6 (151/163)</td>
</tr>
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Stent Fractures:

0% (0/72) NIVL
0% (0/65) PTS
0% (0/137) Total

**ITT PTS N=45**

NIVL N=77 Total N=170

Freedom from TLR & TVR, % (n/N)

81.6 (75/92) 80.0 (157/196) 80.5 (157/194)

Stent Fractures, % (n/N)

0% (0/72) 0% (0/65) 0% (0/137)

**Conclusion**

In this prospective, multicenter trial, the VENOVO Venous Stent when used to treat venous obstructions in the iliac & femoral veins, demonstrated a primary patency benefit compared to a historical control at 12 months while demonstrating significant improvement in both VCSS pain scores and QoL (CIVIQ-20) compared to baseline.

**Secondary Observations (12 Months)**

**ITT N=93**

Freedom from TLR & TVR, % (n/N)

87.6 (78/89)

Stent Fractures, % (n/N)

0% (0/72)

**PTS N=45**

Freedom from TLR & TVR, % (n/N)

98.6 (73/74)

Stent Fractures, % (n/N)

0% (0/65)

**NIVL N=77**

Freedom from TLR & TVR, % (n/N)

92.6 (151/163)

Stent Fractures, % (n/N)

0% (0/137)

Follow up in the VERNACULAR Trial is ongoing through 3 years.