VENOVO Venous Stent: 12-Month Update on the VERNACULAR Trial

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on behalf of the VERNACULAR Trial Investigators
Disclosures

Speaker name: TANG Tjun Yip MD FRCS(Gen)

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☐ I do not have any potential conflict of interest
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
- 6 radiopaque tantalum markers (3 on each end)
- Tri-axial, 0.035” over-the-wire delivery system

Stent Sizes

<table>
<thead>
<tr>
<th>Stent Lengths</th>
<th>10 mm</th>
<th>12 mm</th>
<th>14 mm</th>
<th>16 mm</th>
<th>18 mm</th>
<th>20 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 mm</td>
<td></td>
<td></td>
<td>8F</td>
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<tr>
<td>60 mm</td>
<td></td>
<td></td>
<td></td>
<td>9F</td>
<td></td>
<td></td>
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<tr>
<td>80 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10F</td>
<td></td>
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<tr>
<td>100 mm</td>
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<td>120 mm</td>
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<tr>
<td>140 mm</td>
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<tr>
<td>160 mm</td>
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</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

- RVD\(^3\): 7 mm - 19 mm (visual estimate)

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\(^1\) Clinical Score from the Clinical-Etiology-Anatomy-Pathophysiology (CEAP) Classification

\(^2\) Pain Score from the Venous Clinical Severity Score (VCSS)

\(^3\) Reference Vessel Diameter
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:**
  - **12-Month Primary Patency**: Freedom from target vessel revascularization (TVR) and thrombotic occlusion and stenosis > 50% measured by DUS (VasCore DUS Core Lab)

- **Primary Safety:**
  - **Freedom from MAEs (30-days)**: Including,
    - TVR
    - Device and/or procedure-related death
    - Target limb major amputation
    - Clinically relevant pulmonary embolism
    - Vascular injury requiring intervention
    - Embolization and/or migration 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 Safety and Efficacy Endpoints were compared to literature-derived performance goals*
# Patient Demographics

<table>
<thead>
<tr>
<th>ITT Population</th>
<th>PTS(^1) (N=93)</th>
<th>NIVL(^2) (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/m(^2) ± SD</td>
<td>28.6 ± 6.4</td>
<td>29.1 ± 7.7</td>
<td>28.8 ± 7.0</td>
</tr>
<tr>
<td>Co-Morbidities/Medical History, % (n)</td>
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<td></td>
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<tr>
<td>Varicosis</td>
<td>76.3 (71)</td>
<td>80.5 (62)</td>
<td>78.2 (133)</td>
</tr>
<tr>
<td>May-Thurner Syndrome</td>
<td>37.6 (35)</td>
<td>87.0 (67)</td>
<td>60.0 (102)</td>
</tr>
<tr>
<td>Smoker (Current &amp; Former)</td>
<td>30.1 (28)</td>
<td>39.0 (30)</td>
<td>34.1 (58)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29.0 (27)</td>
<td>36.4 (28)</td>
<td>32.4 (55)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>21.5 (29)</td>
<td>35.1 (27)</td>
<td>27.6 (47)</td>
</tr>
<tr>
<td>Diabetes (Type 2)</td>
<td>5.4 (5)</td>
<td>16.9 (13)</td>
<td>10.6 (18)</td>
</tr>
<tr>
<td>Peripheral Artery Disease</td>
<td>6.5 (6)</td>
<td>15.6 (12)</td>
<td>10.6 (18)</td>
</tr>
</tbody>
</table>

\(^1\) Post-Thrombotic Syndrome  
\(^2\) Non-Thrombotic Iliac Vein Lesion
Lesion Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ITT</th>
<th>PTS (N=93)</th>
<th>NIVL (N=77)</th>
<th>Total (N=170)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Location², %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common Iliac Vein</td>
<td></td>
<td>92.1</td>
<td>97.3</td>
<td>94.5</td>
</tr>
<tr>
<td>External Iliac Vein</td>
<td></td>
<td>58.4</td>
<td>18.9</td>
<td>40.5</td>
</tr>
<tr>
<td>Common Femoral Vein</td>
<td></td>
<td>14.6</td>
<td>2.7</td>
<td>9.2</td>
</tr>
<tr>
<td>Lesion Morphology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Lesion Length, mm ± SD</td>
<td></td>
<td>80.5 ± 42.8</td>
<td>55.2 ± 32.0</td>
<td>67.8 ± 40.0</td>
</tr>
<tr>
<td>Thrombus Present, % (n/N)</td>
<td></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 (3/74)</td>
<td>22.8 (37/162)</td>
<td></td>
</tr>
<tr>
<td>% Diameter Stenosis, mean ± SD</td>
<td></td>
<td>81.0 ± 18.4</td>
<td>69.3 ± 12.6</td>
<td>75.7 ± 17.0</td>
</tr>
</tbody>
</table>

¹ 163 patients had images evaluable by the core lab

² Lesions could occur in more than one vein per patient
## Procedural Data

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</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>
<td></td>
</tr>
<tr>
<td>Number of Stents Implanted</td>
<td>134</td>
<td>85</td>
<td>219¹</td>
<td></td>
</tr>
<tr>
<td>Number of Stents per Patient</td>
<td>1.4</td>
<td>1.1</td>
<td>1.3</td>
<td></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>
<td></td>
</tr>
<tr>
<td>Final % Diameter Stenosis, mean ± SD</td>
<td>16.2 ± 6.8</td>
<td>11.9 ± 4.9</td>
<td>14.2 ± 6.3</td>
<td></td>
</tr>
<tr>
<td>Acute Technical Success¹, % (n/N)</td>
<td>100 (93/93)</td>
<td>100 (77/77)</td>
<td>100 (170/170)</td>
<td></td>
</tr>
<tr>
<td>Acute Procedure Success², % (n/N)</td>
<td>97.8 (91/93)</td>
<td>100 (77/77)</td>
<td>98.8 (168/170)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Successful stent deployment to the intended location with adequate lesion coverage (investigator assessment)

² Technical success plus no MAEs through discharge. Two patients in the PTS group had a revascularization following a DVT (investigator assessment)
Primary Efficacy Endpoint

Primary Patency (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(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Patency, % (90% CI)</td>
<td>81.3% (72.6%, 88.1%)</td>
<td>96.9% (90.6%, 99.5%)</td>
<td>88.3(^2) (82.4%, 94.2(^3))</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Primary patency with VENOVO was greater than a literature-derived performance goal (74%)

1 Proportional analysis
2 Weighted combined patency rate of PTS and NIVL with 55% and 45% weight, respectively. The combined patency was tested against the performance goal of 74%
3 90% confidence intervals from the weighted Z statistics
4 One-sided p-value calculated from the weighted Z statistics
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

Survival Probability

Time to Event (Days)

88.9%
(83.9%, 92.4%)
at 395 days
## Primary Safety Endpoint

### Freedom from MAEs (30 Days)

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<tr>
<th>ITT Population</th>
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<th>NIVL N=77</th>
<th>Total N=170</th>
<th>90% CI</th>
<th>p-value&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedom from MAEs, % (n/N)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>88.2% (82/93)</td>
<td>100% (77/77)</td>
<td>93.5% (159/170)</td>
<td>89.5%, 96.3%</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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

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<sup>1</sup> Proportional analysis

<sup>2</sup> 90% confidence interval calculated using the exact binomial test

<sup>3</sup> P-value computed compared with the performance goal (89%) using a one-sided exact binomial test
Secondary Endpoint: VCSS Pain Score

Mean Improvement from Baseline:
-1.7 (95% CI: -1.8, -1.5) (p < 0.0001)

Paired mean difference in pain score at 12-months compared to baseline (95% CI). A mean difference < 0 and the two-sided p-value (paired t-test) were significant and indicated a shift to lower pain scores.
Secondary Endpoint: CIVIQ-20 Score*

**Significant Shift to Greater Patient Comfort**

Mean Improvement from Baseline: 
-15.7 (95% CI: -18.4, -13.0)  
(p < 0.0001)

Paired mean difference in CIVIQ-20 global score (pain, physical, psychological, and social) at 12-months compared to baseline (95% CI). A mean difference < 0 and the two-sided p-value (paired t-test) indicated a significant shift in overall patient QoL.
Secondary Observations (12 Months)

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Freedom from TLR &amp; TVR, % (n/N)</td>
<td></td>
<td>87.6 (78/89)</td>
<td>98.6 (73/74)</td>
<td>92.6 (151/163)</td>
</tr>
<tr>
<td>Stent Fractures¹, % (n/N)</td>
<td>0% (0/72)</td>
<td>0% (0/65)</td>
<td>0% (0/137)</td>
<td></td>
</tr>
</tbody>
</table>

Descriptive Statistics. No formal hypothesis testing

¹ An AP and Lateral x-ray for each evaluated stent were submitted to the Core Lab for analysis. 137 patients had x-rays that could be evaluated by the Yale core lab for stent fractures.
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.

VERNACULAR Trial Summary:
• 30-Day Freedom from MAEs: 93.5%
• 12-Month Primary Patency: 88.3%
• 12-Month TLR Rate: 7.4%
• Stent Fractures (Core Lab Analyzed at 12 Months): 0%

Follow up in the VERNACULAR Trial is ongoing through 3 years
SGH Deep Venous Stenting Program

- Over 70 cases since March 2017
- 32 patients with Venovo stents
- 25/32 female (78%); mean age 67 years
- 27/32 (84%) NTIVL
- 100% technical success
- 97% primary patency rate
- 1 in stent partial thrombosis; reintervention to remove clot and reline it
- No stent fractures
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