# VERNACULAR TRIAL – 3 YEAR UPDATE

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On behalf of
the VERNACULAR Trial Investigators

**Disclosure**

Speaker name: Michael Lichtenberg

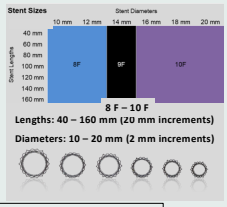
I have the following potential conflicts of interest to report:

- ❑ Receipt of grants/research support
- ❑ Receipt of honoraria and travel support
- ❑ Participation in a company-sponsored speaker bureau
- ❑ Employment in industry
- ❑ Shareholder in a healthcare company
- ❑ Owner of a healthcare company

❑ I do not have any potential conflict of interest

## 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

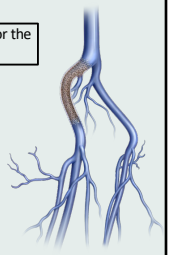



Indication for Use: Treatment of symptomatic iliofemoral venous outflow obstruction

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

## VERNACULAR Study Overview

Objective: Assess the performance of the Venovo Venous Stent for the treatment of iliofemoral vein outflow obstructions



- **Design:** Prospective, Multicenter, Non-Randomized, Single-Arm
  - Intention-to Treat Population: 170 patients
  - International Multicenter: 22 sites in USA, Europe, and Australia
- **Independent Analysis:**
  - Venographic & radiographic assessment: Yale Core Lab
  - Duplex Ultrasound (DUS) evaluation: VasCore
  - Clinical Events Committee (CEC): reviewed all adverse events
  - Data Safety Monitoring Board (DSMB): assessed overall patient safety

## VERNACULAR Study Investigators

Principal Investigator: Michael Dake

Co-Principal Investigator (Europe): Gerard O'Sullivan

U.S. Sites

| Investigator | Site Name | State |
|---|---|---|
| Jeffrey Apple | Cardiothoracic and Vascular Surgeons | TX |
| Robert Lookstein | Mount Sinai Medical Center | NY |
| John Mullins | Cox Medical Centers | MO |
| David Dexter | Sentara Norfolk General Hospital | VA |
| Nicolas Shammas | Midwest Cardiovascular Research Found. | IA |
| Shadi Abu-Halimah | CAMC Health Education & Res Institute | WV |
| Brian Ferris | Lake Washington Vascular | WA |
| Barbara Karenko | Metro Helath Hospital | MI |
| Robert Mendes | NC Heart and Vascular Research | NC |
| Khanjan Nagarsheth | Rutgers University | NJ |
| Robert Attaran | Yale University | CT |
| Ronald Morford | Centra Health | VA |
| Paul Gagne | Vascular Breakthroughs | CT |

OUS Sites

| Investigator | Site Name | Country |
|---|---|---|
| Thomas Zeller | Universitäts-Herzzentrum Freiburg-Bad Krozingen | Germany |
| Michael Lichtenberg | Klinikum Arnsberg (Hochsauerland) | Germany |
| Gerard O'Sullivan | University Hospital Galway | Ireland |
| Steven Black | Guy's & St. Thomas' Hospital | United Kingdom |
| Michiel de Haan | MUMC Maastricht | The Netherlands |
| Luis Miguel Izquierdo Larrosca | Fundacion de investigación | Spain |
| Houman Jalaie | Uniklinik RWTH | Germany |
| Steven Dubenec | Royal Prince Alfred Hospital | Australia |
| Patrice Mwipatayi | JMLS Medical Services | Australia |

22 Investigative Sites: U.S., Europe, and Australia

## VERNACULAR Study Criteria

**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)

**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

[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

## Patient Demographics

ITT[1] Population / Subgroups

| Demographic Criteria | Total (N=170) | PTS[2] (N=93) | NIVL[3] (N=77) |
|---|---|---|---|
| Mean Age, years ±SD | 52.1 ± 15.3 | 49.8 ± 15.0 | 55.0 ± 15.4 |
| Male/Female, %/% | 37.2/62.9 | 45.2/54.8 | 27.3/72.7 |
| Mean BMI, kg/m² ±SD | 28.8 ± 7.0 | 28.6 ± 6.4 | 29.1 ± 7.7 |
| Co-Morbidities/Medical History, % (n) | | | |
| Varicosis | 78.2 (133) | 76.3 (71) | 80.5 (62) |
| May-Thurner Syndrome | 60.0 (102) | 37.6 (35) | 87.0 (67) |
| Smoker (Current & Former) | 34.1 (58) | 30.1 (28) | 39.0 (30) |
| Hypertension | 32.4 (55) | 29.0 (27) | 36.4 (28) |
| Dyslipidemia | 27.6 (47) | 21.5 (20) | 35.1 (27) |
| Diabetes (Type 2) | 10.6 (18) | 5.4 (5) | 16.9 (13) |
| Peripheral Artery Disease | 10.6 (18) | 6.5 (6) | 15.6 (12) |

ITT population = 55% PTS; 45% NIVL

[1] Intent To Treat Population; [2]Post-Thrombotic Syndrome; [3] Non-Thrombotic Iliac Vein Lesion

## Lesion Characteristics & Procedural Data

| Lesion Criteria | Total (N=170) | PTS (N=93) | NIVL (N=77) |
|---|---|---|---|
| Lesion Location[1], % | | | |
| Common Iliac Vein | 94.5 | 92.1 | 97.3 |
| External Iliac Vein | 40.5 | 58.4 | 18.9 |
| Common Femoral Vein | 9.2 | 14.6 | 2.7 |
| Lesion Morphology | | | |
| Mean Lesion Length, mm ±SD | 67.8 ± 40.0 | 80.5 ± 42.8 | 55.2 ± 32.0 |
| Thrombus Present, % (n/N) | 8.6 (14/162) | 14.8 (13/88) | 1.4 (1/74) |
| No Blood Flow (Occluded), % (n/N) | 22.8 (37/162) | 38.6 (34/88) | 4.1 (3/74) |
| Number of Stents, N | 219 | 134 | 85 |
| Number of Stents per Patient | 1.3 | 1.4 | 1.1 |
| Mean Stented Length, mm ±SD | 109.8 ± 52.7 | 130.2 ± 56.9 | 85.3 ± 33.7 |
| Acute Technical Success[2], % (n/N) | 100 (170/170) | 100 (93/93) | 100 (77/77) |
| Acute Procedure Success[3], % (n/N) | 98.8 (168/170) | 97.8 (91/93) | 100 (77/77) |

[1] Lesions could occur in more than one vein per patient; [2]Successful stent deployment to the intended location with adequate lesion coverage (investigator assessment);
[3] Technical success plus no MAEs through discharge. Two patients in the PTS group had a revascularization following a DVT (investigator assessment)

## VERNACULAR Study: Primary Endpoints

Safety: Freedom from MAEs (30 Days)

| | ITT (N=170) | 90% CI | Performance Goal | p-value[1] |
|---|---|---|---|---|
| Freedom from MAEs % (n/N) | 93.5% (159/170) | [89.5%, 96.3%] | 89% | 0.03 |

Freedom from MAEs with VENOVO was statistically significant when compared to the literature-derived performance goal

Efficacy: 12-Month Primary Patency*

| | ITT (N=170) | 90% CI | Performance Goal | p-value[2] |
|---|---|---|---|---|
| Primary Patency % (n/N) | 88.6% (133/150) | [82.8%, 94.4%] | 74% | <0.0001 |

*Freedom from target vessel revascularization (TVR) and thrombotic occlusion and stenosis > 50% measured by DUS Core Lab

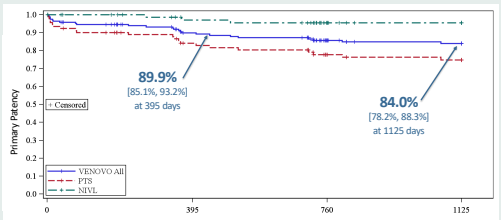
Primary Patency with VENOVO was statistically significant when compared to the literature-derived performance goal

[1] P-value computed compared with the performance goal (89%) using a one-sided exact binomial test

[2] One-sided p-value calculated from the weighted Z-statistics

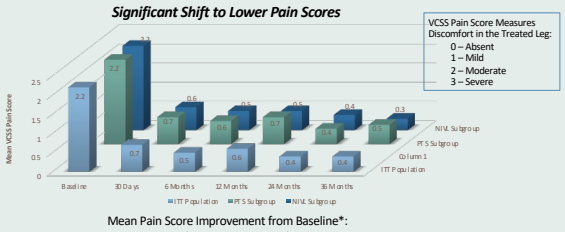
## Secondary Endpoints: Final 36 Month Data

## Primary Patency Through 36 Months




Kaplan-Meier survival analysis – 1125 days is the end of the 36-month follow-up interval

## VCSS Pain Score through 36 Months

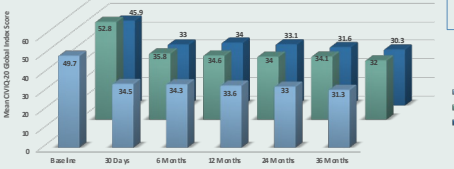



Mean Pain Score Improvement from Baseline*:
-1.8 (95% CI: -1.95, -1.66)
*Paired mean difference in pain score at 36 months compared to baseline (95% CI).

## CIVIQ-20 Score through 36 Months

***Significant Shift to Greater Patient Comfort***

Mean Global Index Improvement from Baseline*:
-16.8 (95% CI: -20.07, -13.54)




CIVIQ-20 Global Index: A composite of 20 questions, each scored from 1 (lowest) to 5 (severe) discomfort.
Components:
- Pain
- Physical
- Psychological
- Social

*Paired mean difference in CIVIQ-20 global score (pain, physical, psychological, and social) at 36 months compared to baseline (95% CI).

## VERNACULAR Study: Final Data at 3 Years

**ITT Population**

| Observations | 12 Month | 24 Months | 36 Months |
|---|---|---|---|
| Freedom from TLR, (95% CI) | 92.6% [87.5, 96.1] | 89.4% [83.6, 93.7] | 88.1 [81.8, 92.8] |
| Primary Patency, (90% CI) | 88.6% [82.8, 94.4][1] | 84.4% [78.6, 89.1][2] | 79.5% [72.4, 85.4][2] |
| Stent Fractures, (n/N) | 0% (0/137) | 0% (0/128) | 0% (0/98)[3] |

Descriptive statistics - No formal hypothesis testing

[1] Weighed primary patency rate (proportional analysis) – 90% CI from weighted Z-statistics
[2] Proportional analysis; Unweighted CI is estimate by exact binomial method
[3] 98 patients had AP and lateral radiographs that could be evaluated by the Yale core lab at 36 months

Follow up at 3 years was impacted & delayed by the COVID-19 pandemic 3-year follow up: 75.3% (128/170 patients)

## Arnsberg Registry – VENOVO® Stent

| | |
|---|---|
| Study | Assess safety and effectiveness of venous stent placement through 36 months in patients with non-thrombotic iliac vein lesions (NIVL) and post-thrombotic (PTS) iliac vein lesions |
| Design | **Investigator-initiated**, ongoing prospective, single arm, single center, non-randomized registry |
| Endpoints | Primary patency at 12 months; Clinical outcome at 12 months |
| Primary Investigators | Dr. Michael Lichtenberg<br>Dr. Rick de Graaf |
| Subjects | 80 subjects; 50 (63%) PTS and 30 (37%) NIVL |

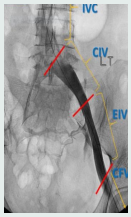
Michael Lichtenberg et al. Venovo venous stent in the treatment of non-thrombotic or post-thrombotic iliac vein lesions- short-term results from the Arnsberg venous registry. Vasa (2019), 48 (2), 1–6.

## Arnsberg Registry – VENOVO® Cohort

| VENOVO® Baseline Scores | |
|---|---|
| CEAP | |
| 3 | 41 (51%) |
| 4-6 | 38 (48%) |

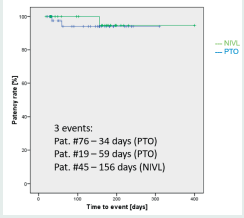
Nearly 50% of the lesions had a CEAP score ≥ 4 (complex lesions) and more than 20% involved the entire iliofemoral segment

| VENOVO® Lesion Location | |
|---|---|
| Left | **56 (70%)** |
| CIV | 30 (38%) |
| CIV + EIV + CFV | 18 (22%) |
| EIV + CFV | 5 (6%) |
| CFV | 3 (4%) |
| Right | **18 (23%)** |
| CIV | 3 (4%) |
| CIV + EIV + CFV | 14 (18%) |
| EIV + CFV | 1 (1%) |
| CFV | N/A |




Stented length: 134 mm

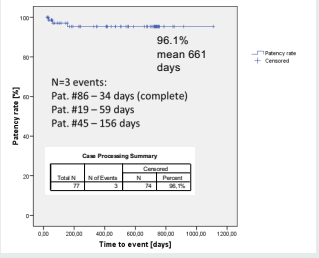
## Arnsberg Registry – VENOVO® Cohort



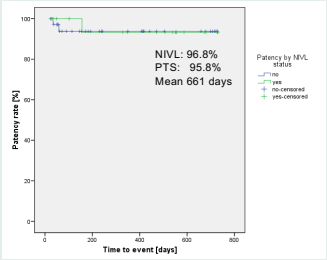

| Patency Results by Duplex | | |
|---|---|---|
| All Patients | | |
| | Primary | Secondary |
| 1-M (77/80) | 98% | 100% |
| 6-M (59/80) | 97% | 100% |
| 12-M (52/80) | 96% | 97% |

| Patency Results by Duplex | | |
|---|---|---|
| By Etiology @ 12 Months (n = 52) | | |
| | Primary | Secondary |
| NIVL | 97% | 100% |
| PTS | 96% | 95% |

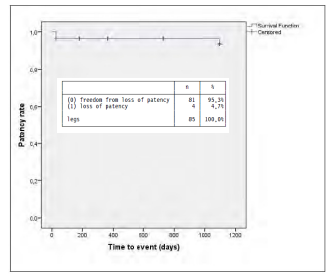
## 24-Months Overall Patency Results



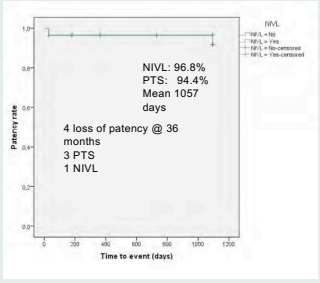
## NIVL vs. PTS Primary Patency After 24-Months



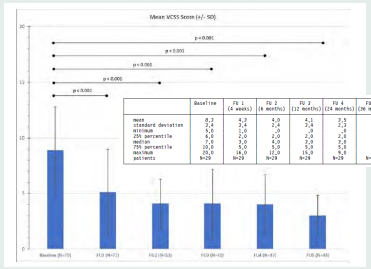

## 36-Months Overall Patency Results



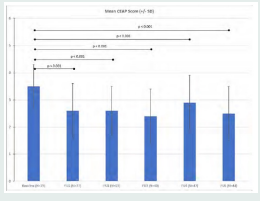

## NIVL vs. PTS Primary Patency After 24-Months




## VCSS during follow-up period



## CEAP score during follow-up period



| | Baseline | FU 1 (6 weeks) | FU 2 (6 months) | FU 3 (12 months) | FU 4 (24 months) | FU 5 (36 months) |
|---|---|---|---|---|---|---|
| mean | 3,6 | 2,3 | 2,4 | 2,4 | 2,0 | 2,5 |
| standard deviation | 2,0 | 1,0 | 1,0 | 1,0 | 2,0 | 2,0 |
| minimum | 2,0 | 1,0 | 1,0 | 1,0 | 2,0 | 2,0 |
| 25% percentile | 3,0 | 2,0 | 2,0 | 2,0 | 2,0 | 2,0 |
| median | 3,0 | 2,0 | 2,0 | 2,0 | 2,0 | 2,0 |
| 75% percentile | 4,5 | 2,0 | 2,0 | 2,0 | 2,0 | 2,0 |
| maximum | 8,0 | 5,0 | 4,0 | 5,0 | 5,0 | 5,0 |

## VERNACULAR Study Summary

Use of the VENOVO Venous Stent to treat iliofemoral vein obstructions, demonstrated:

- Primary patency benefit compared to a historical control ($p < 0.0001$)
- VCSS pain scores and QoL (CIVIQ-20) improved compared to baseline ($p < 0.0001$)

**VERNACULAR Trial – Final Data at 3 Years:**

- Improvement in pain from baseline (VCSS pain score)
- Improvement in overall patient comfort compared to baseline (CIVIQ-20)
- Primary Patency: 79.5% (84% K-M)
- Stent Fractures (Core Lab Analyzed): 0%

Venovo has received PMDA approval in Japan and will launch soon