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

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Disclosure

Speaker name: Michael D. Dake

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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

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

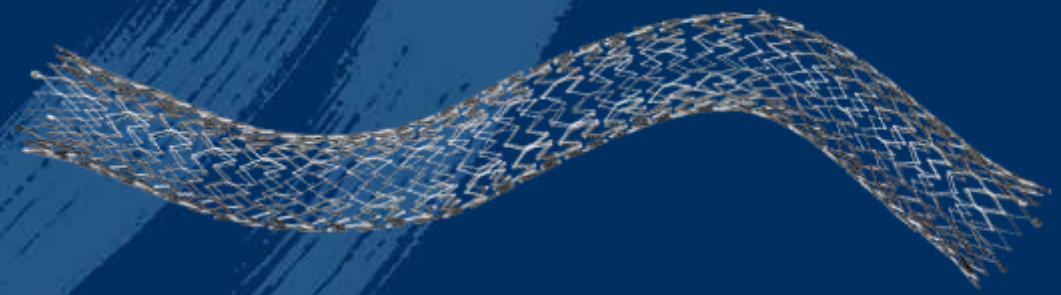
Principal Investigator: Michael Dake

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
- 6 radiopaque tantalum markers (3 on each end)
- Tri-axial, 0.035” over-the-wire delivery system

Stent Sizes

Stent Lengths	Stent Diameters					
	10 mm	12 mm	14 mm	16 mm	18 mm	20 mm
40 mm	8F		9F	10F		
60 mm						
80 mm						
100 mm						
120 mm						
140 mm						
160 mm						

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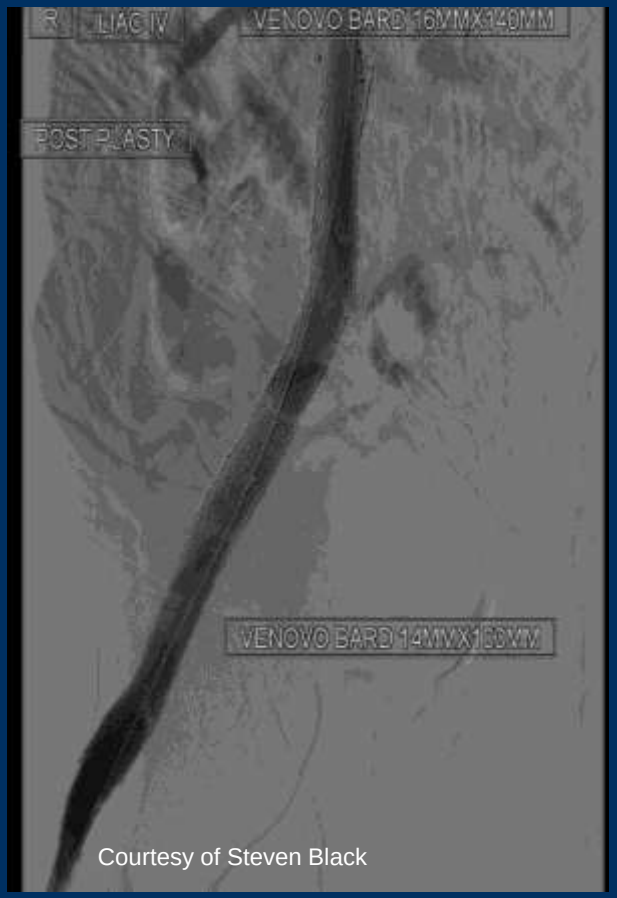
Key Inclusion Criteria

- 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)



Courtesy of Steven Black

[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 $\geq$ 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

* Primary Safety and Efficacy Endpoints were compared to literature-derived performance goals

- **Hypothesis-Tested Secondary Endpoints:**
  - **VCSS Pain Score & Chronic Venous Insufficiency Questionnaire (CIVIQ-20):**
    - ✓Mean difference between baseline & 12 months

Patient Demographics

ITT Population	PTS[1] (N=93)	NIVL[2] (N=77)	Total (N=170)
Mean Age, years ± SD	49.8 ± 15.0	55.0 ± 15.4	52.1 ± 15.3
Male/Female, %/%	45.2/54.8	27.3/72.7	37.2/62.9
Mean BMI, kg/m^2 ± SD	28.6 ± 6.4	29.1 ± 7.7	28.8 ± 7.0
Co-Morbidities/Medical History, % (n)			
Varicosis	76.3 (71)	80.5 (62)	78.2 (133)
May-Thurner Syndrome	37.6 (35)	87.0 (67)	60.0 (102)
Smoker (Current & Former)	30.1 (28)	39.0 (30)	34.1 (58)
Hypertension	29.0 (27)	36.4 (28)	32.4 (55)
Dyslipidemia	21.5 (29)	35.1 (27)	27.6 (47)
Diabetes (Type 2)	5.4 (5)	16.9 (13)	10.6 (18)
Peripheral Artery Disease	6.5 (6)	15.6 (12)	10.6 (18)

[1] Post-Thrombotic Syndrome

[2] Non-Thrombotic Iliac Vein Lesion

Lesion Characteristics

ITT	PTS (N=93)	NIVL (N=77)	Total (N=170)[1]
Lesion Location[2], %			
Common Iliac Vein	92.1	97.3	94.5
External Iliac Vein	58.4	18.9	40.5
Common Femoral Vein	14.6	2.7	9.2
Lesion Morphology			
Mean Lesion Length, mm ± SD	80.5 ± 42.8	55.2 ± 32.0	67.8 ± 40.0
Thrombus Present, % (n/N)	14.8 (13/88)	1.4 (1/74)	8.6 (14/162)
No Blood Flow (Occluded), % (n/N)	38.6 (34/88)	4.1 (3/74)	22.8 (37/162)
% Diameter Stenosis, mean ± SD	81.0 ± 18.4	69.3 ± 12.6	75.7 ± 17.0

[1] 163 patients had images evaluable by the core lab

[2] Lesions could occur in more than one vein per patient

Procedural Data

ITT	PTS (N=93)	NIVL (N=77)	Total (N=170)
Mean Procedure Time, min ± SD	64.7 ± 32.9	48.8 ± 18.0	57.5 ± 28.2
Number of Stents Implanted	134	85	219[1]
Number of Stents per Patient	1.4	1.1	1.3
Mean Stented Length, mm ± SD	109.2 ± 49.8	86.0 ± 45.2	100.6 ± 49.1
Final % Diameter Stenosis, mean ± SD	16.2 ± 6.8	11.9 ± 4.9	14.2 ± 6.3
Acute Technical Success[1], % (n/N)	100 (93/93)	100 (77/77)	100 (170/170)
Acute Procedure Success[2], % (n/N)	97.8 (91/93)	100 (77/77)	98.8 (168/170)

[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)

ITT Population	PTS N=93	NIVL N=77	Total N=170	p-value[4]
Primary Patency, % (90% CI)	81.3% (72.6%, 88.1%)	96.9% (90.6%, 99.5%)	88.3%[2] (82.4%, 94.2%)[3]	<0.0001

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

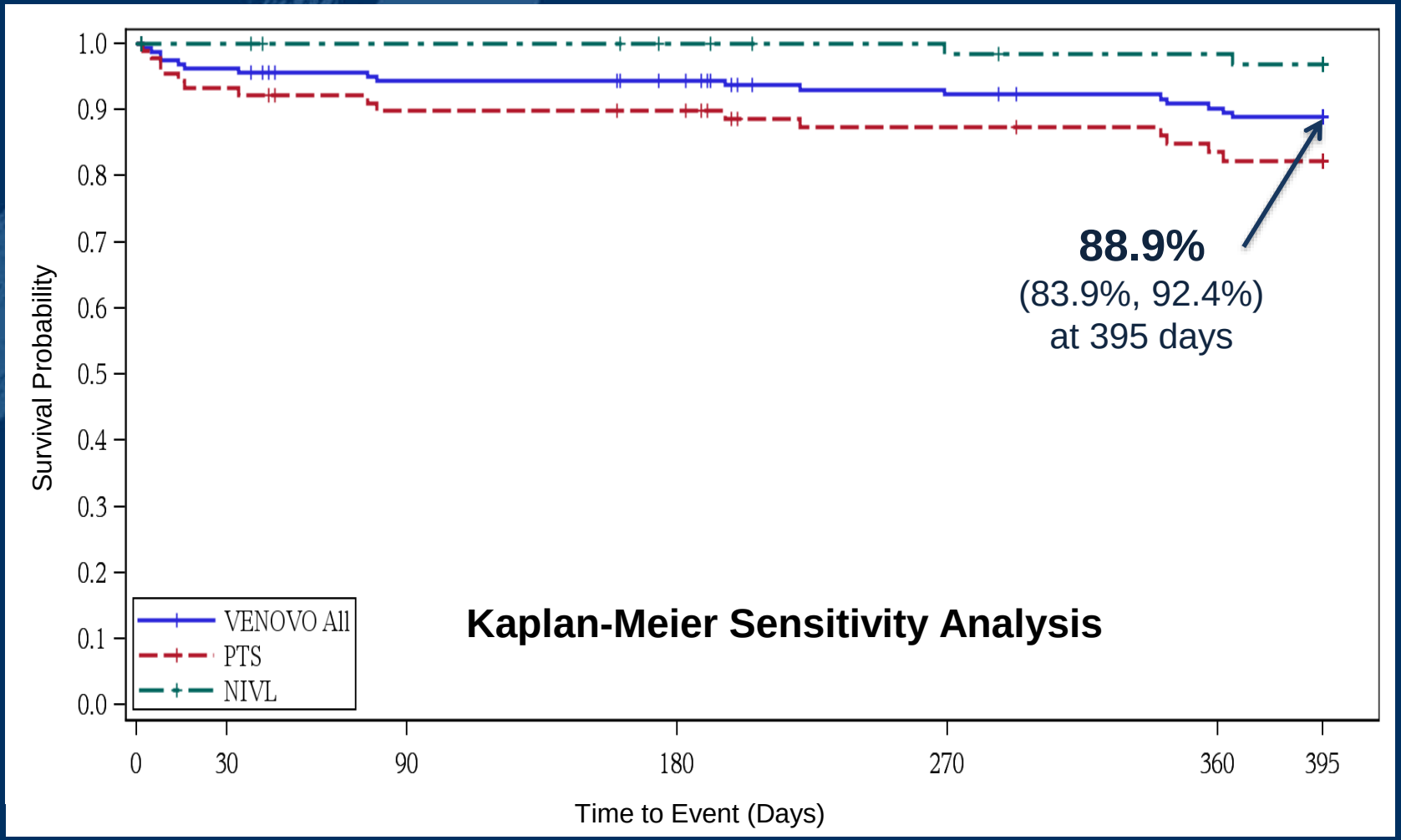
[1] Proportional analysis

[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



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

Primary Safety Endpoint

Freedom from MAEs (30 Days)

ITT Population	PTS N=93	NIVL N=77	Total N=170	90% CI[2]	p-value[3]
Freedom from MAEs, % (n/N)[1]	88.2% (82/93)	100% (77/77)	93.5% (159/170)	89.5%, 96.3%	0.03

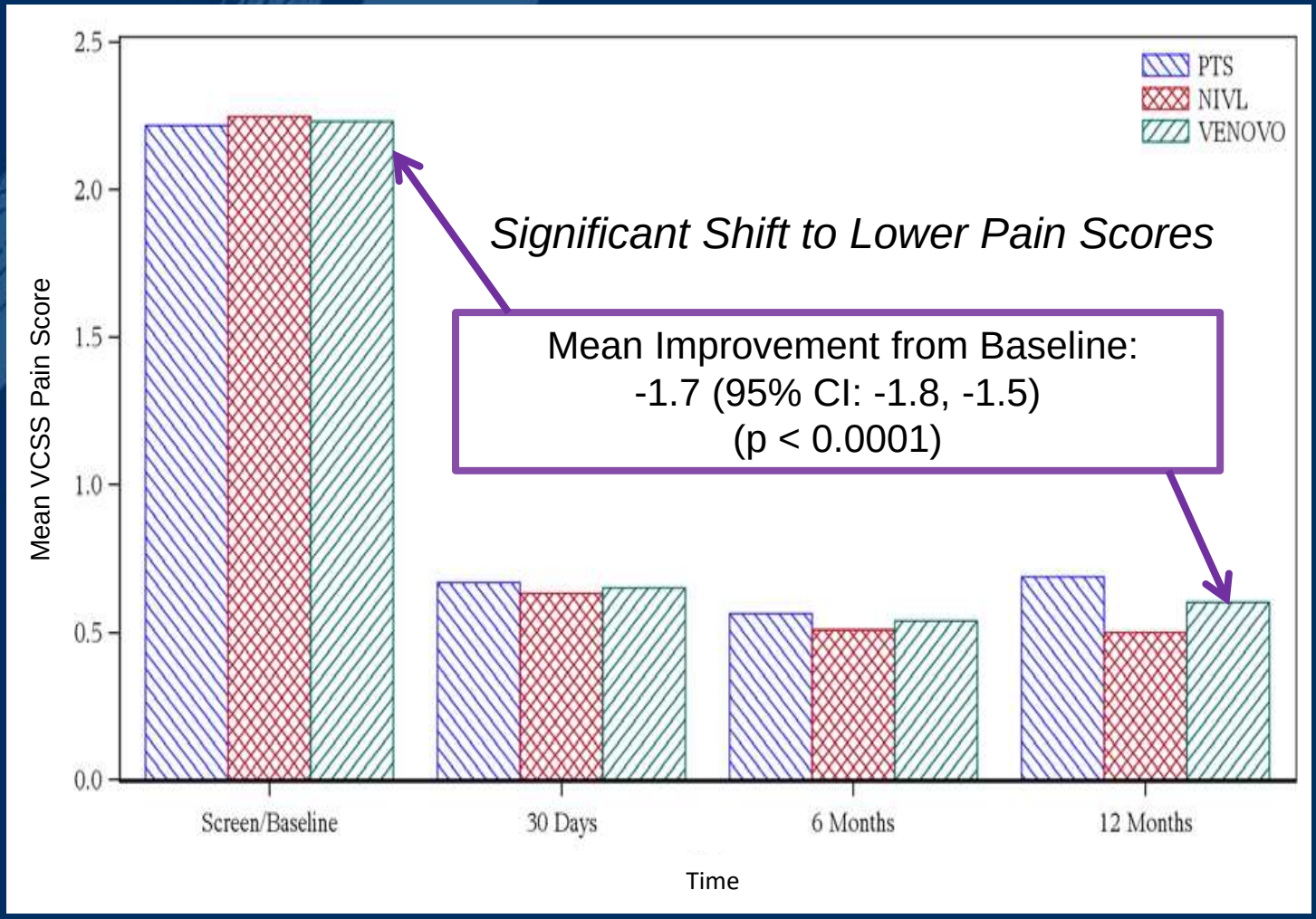
Freedom from MAEs with VENOVO was *better than* a literature-derived performance goal (89%)

[1] Proportional analysis

[2] 90% confidence interval calculated using the exact binomial test

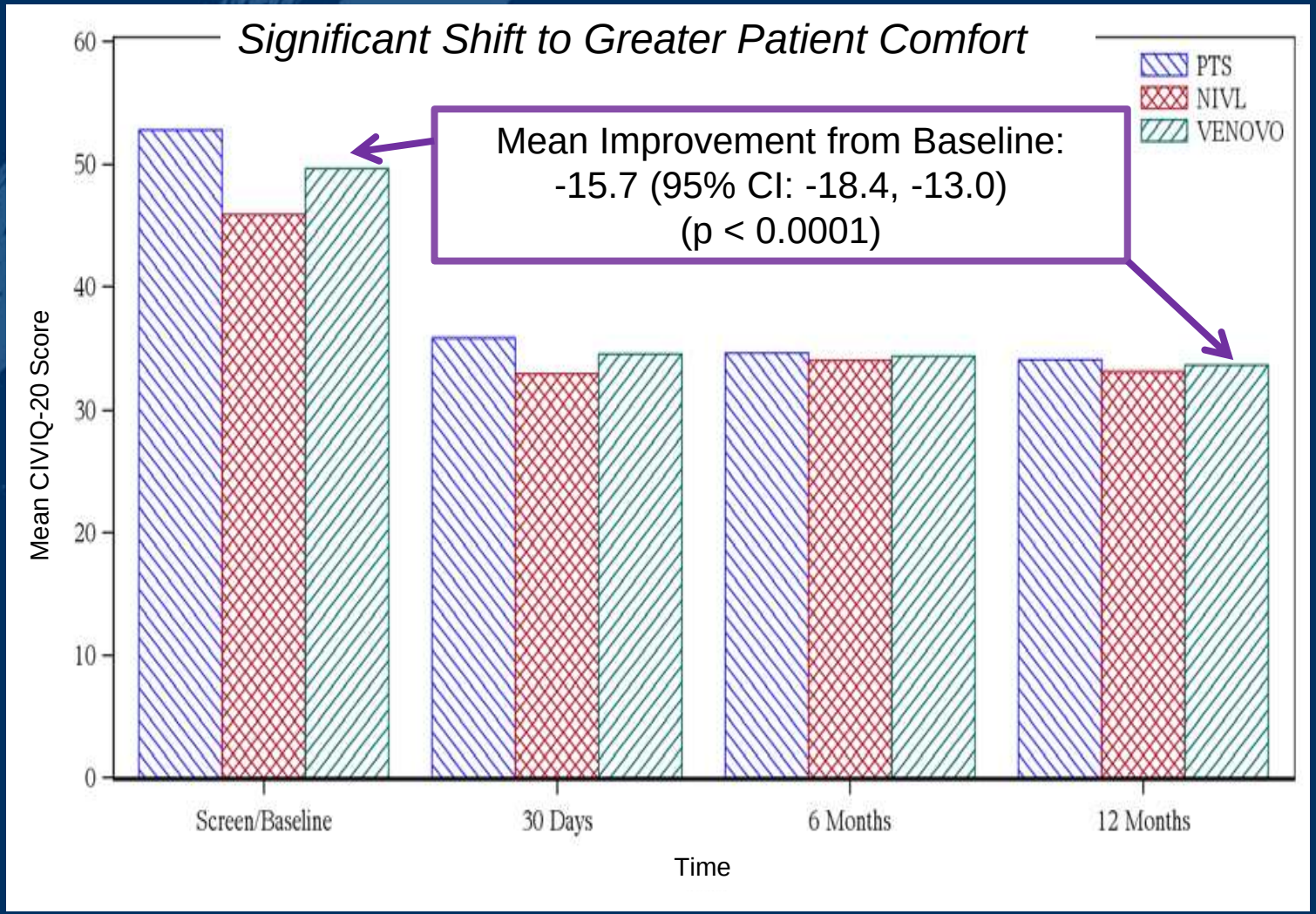
[3] P-value computed compared with the performance goal (89%) using a one-sided exact binomial test

Secondary Endpoint: VCSS Pain Score



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*



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)

ITT	PTS (N=93)	NIVL (N=77)	Total (N=170)
Freedom from TLR & TVR, % (n/N)	87.6 (78/89)	98.6 (73/74)	92.6 (151/163)
Stent Fractures[1], % (n/N)	0% (0/72)	0% (0/65)	0% (0/137)

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

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