VIRTUS: Trial Design and Primary Endpoint Results

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- IMPORTANT INFORMATION: These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician's professional judgment in light of all available information for the case at hand.
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Disclosure

Speaker name:

Mahmood K. Razavi

I have the following potential conflicts of interest to report:

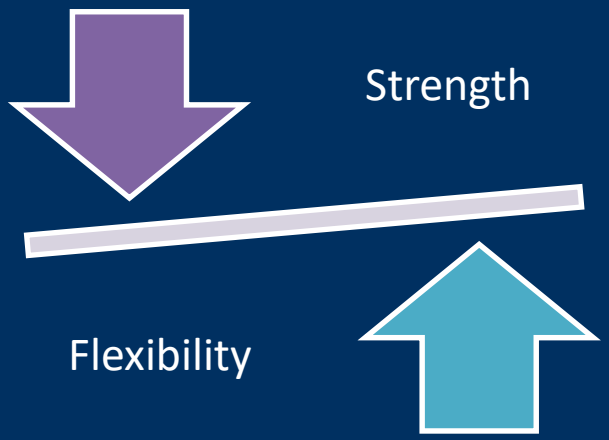
- [X] Consulting (BSC/Veniti)
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

Desired Venous Stent Attributes

- Crush resistant & sufficient radial force across the length of stent
- Sufficient wall coverage
- Flexibility sufficient to resist kink at physiological angles
- Durability allowing repeated shortening, twisting, and bending at the groin
- Minimal foreshortening on deployment and balloon dilation
- Predictable, consistent deployment
- Ability to visualize under fluoroscopy

Goal:
balance strength, flexibility, and lumen quality



Venous Stent Trials

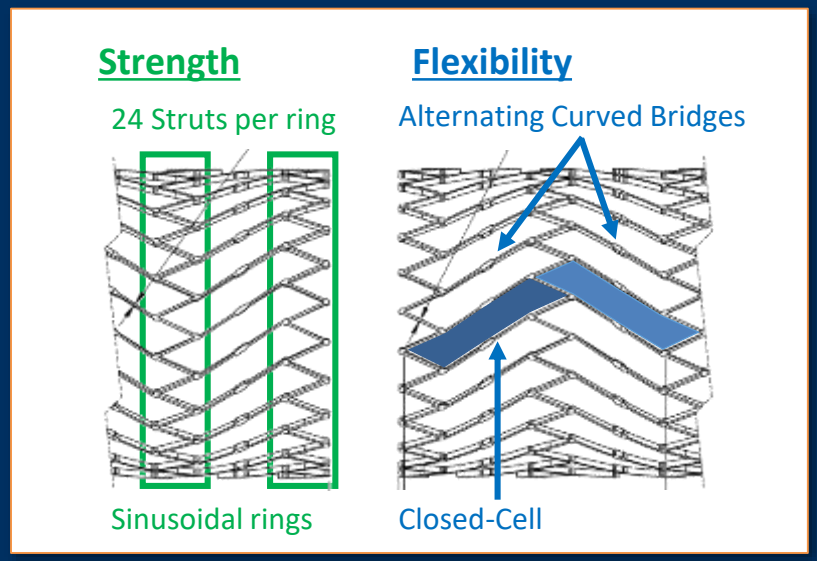
	VICI (Veniti/Boston Scientific)	Zilver™ Vena™ (Cook)	VENOVO (Bard)	ABRE (Medtronic)
CE Mark/ FDA Approval	✓/ -	✓/ -	✓/ -	✓/ -
Trial Name	VIRTUS	VIVO	VERNACULAR	ABRE
Design	Multi-center, single arm	Multi-center, single arm	Multi-center, single arm	Multi-center, single arm
N	170 (pivotal cohort)	243	170	200
Efficacy endpoint	**12M Primary patency** Freedom from: • Reintervention • Occlusion, thrombosis • In-stent restenosis >50% by **venogram**	**12M Primary patency**	**12M Primary patency** Freedom from: • Reintervention • Occlusion, thrombosis • In-stent restenosis >50% by **DUS**	**12M Primary patency** Freedom from: • Clinically-driven TLR • Occlusion • In-stent restenosis >50%
Eligibility	• CEAP "C" ≥3 OR VCSS Pain Score ≥2 • Iliofemoral occlusive disease • ≥50% reduction in target vessel lumen diameter (venogram)	• CEAP "C" ≥3 OR VCSS Pain Score ≥2 • Symptomatic venous outflow obstruction in one iliofemoral venous segment	• CEAP "C" ≥3 OR VCSS Pain Score ≥2 • Iliofemoral occlusive disease (DVT, PTS, May-Thurner, or combination) • Venous outflow obstruction in the iliofemoral segment ≥50%	• Symptomatic iliofemoral venous outflow obstruction
clinicaltrials.gov	NCT02112877	NCT01970007	NCT02655887	NCT03038438

VICI Venous Stent is an investigational device limited by U.S. law to investigational use only. Not available for sale in the U.S. VIRTUS- clinicaltrials.gov & Razavi M, et al. J Vasc Surg Venous Lymphat Disord. 2017. pii: S2213-333X(17)30509-7. doi:10.1016/j.jvsv.2017.10.014. VIVO- clinicaltrials.gov
VERNACULAR- Jalaie H, LINC 2018. ABRE- Murphy E, VEITH 2017 (http://www.veithsymposium.org/abstracts/2017/vei/1160.pdf)

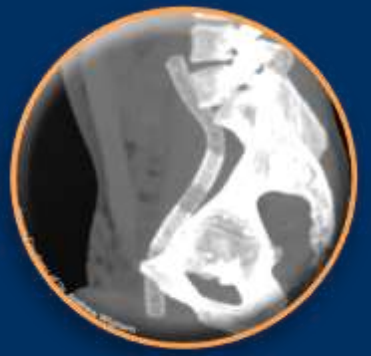
VICI Venous Stent™ System

Designed for:

• Strength	High crush resistance
• Flexibility	Multi-directional
• Crush Resistance (end-to-end)	Lumen 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



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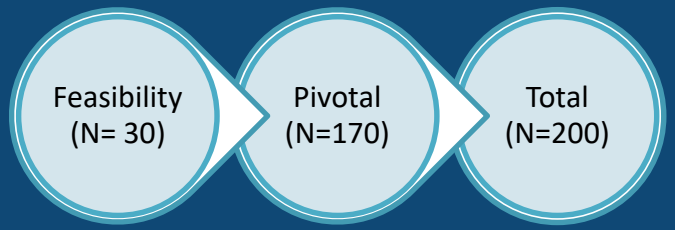
VIRTUS Trial Design

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**
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



- **Results for the pivotal cohort (N=170) are presented here**

VIRTUS Endpoints

Primary Effectiveness Endpoint	**Primary patency rate at 12 months post-intervention** • Freedom from occlusion by thrombosis and • Freedom from surgical or endovascular intervention on target vessel which are found to have re-stenosis or stent occlusion to maintain patency and • Freedom from in-stent stenosis more than **50% by venogram**
Primary Safety Endpoint	Composite endpoint of **freedom from any Major Adverse Event** within 30 days of index procedure (adjudicated by a Clinical Events Committee) • Device or procedure-related death • Device or procedure-related bleeding at the target vessel and/or the target lesion or at the access site • Device or procedure-related arterial or venous injury occurring in the target vessel segment and/or target lesion location or at the access site • Device or procedure related acute DVT outside of the target vein segment • Clinically significant pulmonary embolism • Embolization of stent

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:

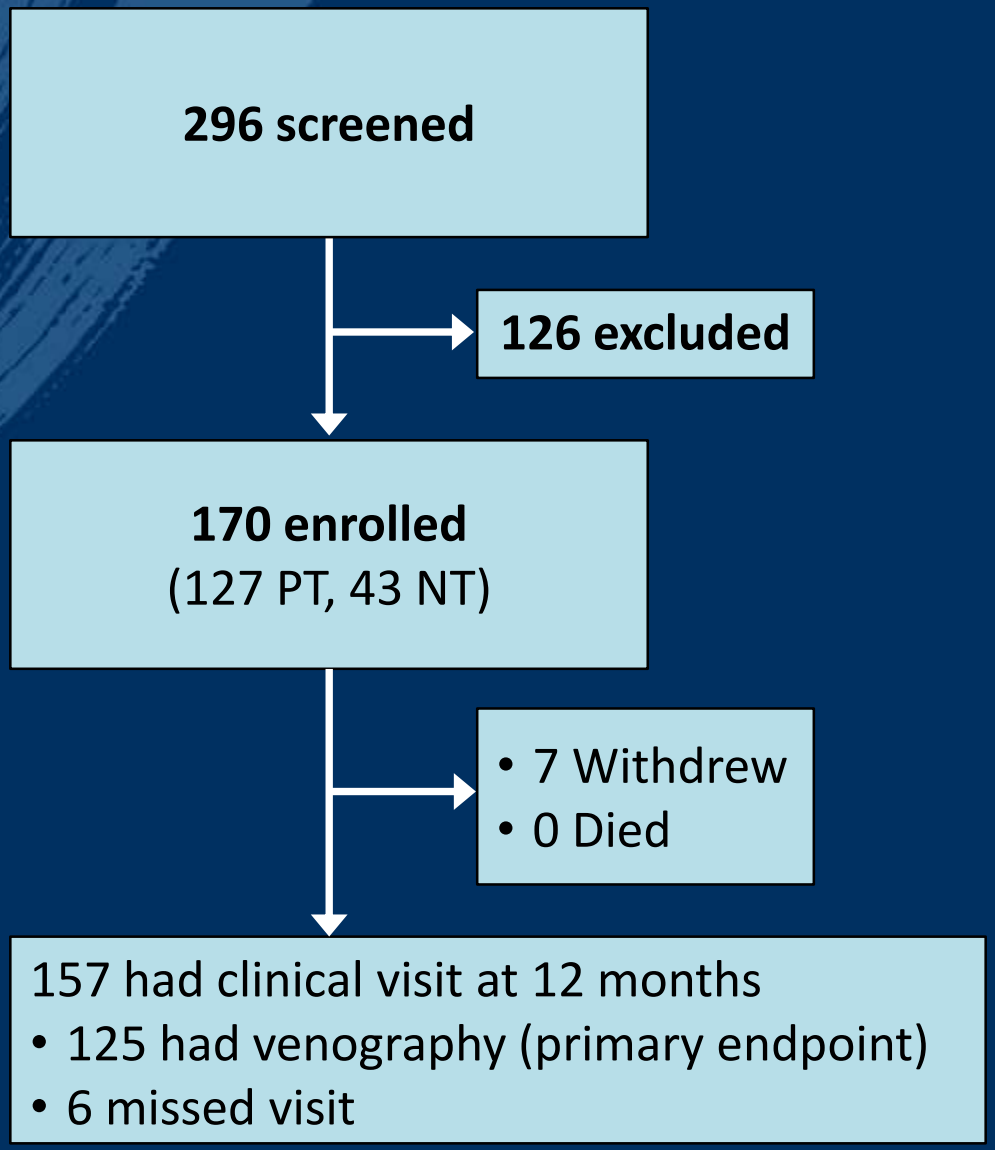
CEAP "C" ≥3 OR VCSS Pain ≥2

Imaging Schedule

	Pre-stent	Post-stent	12 Months
Venography	✓	✓	✓ Patency endpoint
DUS		✓ Discharge or 3d post-procedure	✓
IVUS	✓	✓	✓

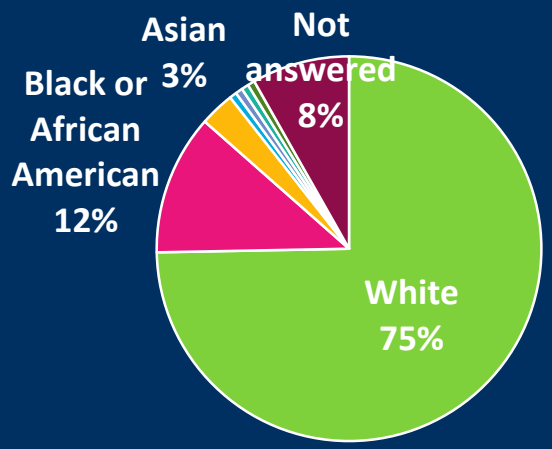
VIRTUS

Patient Flow



Baseline Patient Characteristics

Demographics and Medical History	N=170
Age, y	54.4±16.2
Male/Female	43.5%/56.5%
Diabetes	17.1%
Smoking History	
Current	12.4%
Former	24.1%
Thromboembolic disease	76.5%
Pulmonary embolism	21.5%
Deep vein thrombosis	91.5%
Coagulation disorder	13.5%
Hypertension	40.0%
Peripheral vascular disease	17.1%
Cancer	10.6%
Coronary artery disease	8.2%
Cerebrovascular accident	5.9%
Renal disease	4.7%
Hepatic disease	2.9%
PTA/stent	2.4%
CABG	2.4%
CHF	2.4%



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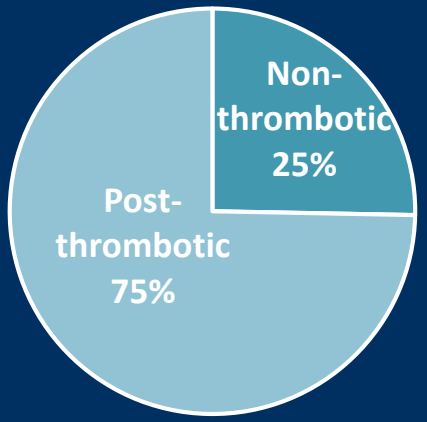
Baseline Patient Characteristics

Clinical Assessment	N=170
Obstruction present in:	
Left leg	85.3%
Right leg	14.1%
Both legs	0.6%
% Stenosis	77.5%
Total Occlusion	31.2%
Lesion Length, mm	111.3 ±65.8
CEAP "C" Assessment	
0	1.2%
1	0%
2	1.2%
3	26.5%
4	45.9%
5	12.9%
6	12.4%
Target Limb VCSS Severity	
VCSS ≤3 (Mild)	8.2%
VCSS 4-7 (Moderate)	26.0%
VCSS ≥8 (Severe)	65.8%

Etiology



Lesion Location

CIV only 21.2%

CIV and EIV 34.7%

CIV, EIV, and CFV 31.8%

EIV only 6.5%

EIV and CFV 4.1%

CFV only 1.8%

CFV, common femoral vein; CIV, common iliac vein; EIV, external iliac vein.

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Procedures

N=170	
Stented length, mm	Median 120 (range 60-300) Mean 149.8 ± 55.7
Procedural technical success	98.8%
Post-procedure stenosis	
Venogram	4.6% ± 7.8%
IVUS	4.2% ± 7.6%

Procedural technical success defined as final residual target vessel diameter stenosis of ≤50% as measured by venogram.

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12 Month Patency

Endpoint	Rate
Primary Patency (primary endpoint[a])	**84.0%**

- Primary endpoint was met: Primary patency rate exceeded the performance goal of 72.1% ($p<0.0001$)[a,b]
- Primary patency based on venography only[c]
  - 79.8% Post-thrombotic
  - 96.2% Non-thrombotic

Primary patency defined as stenosis of target lesion ≤50% (based on venogram) without surgical or endovascular intervention on target vessel to restore patency.

[a]For the primary endpoint, patients who did not have venography performed at 12 months had their result imputed by random selection from subjects with a venogram result who had the same etiology and the same DUS outcome (if available).

[b]Primary effectiveness analysis based on the combined result from 15 imputations; t-statistic 4.0; $p<0.0001$.

[c]12-month venograms were available for 125 patients.

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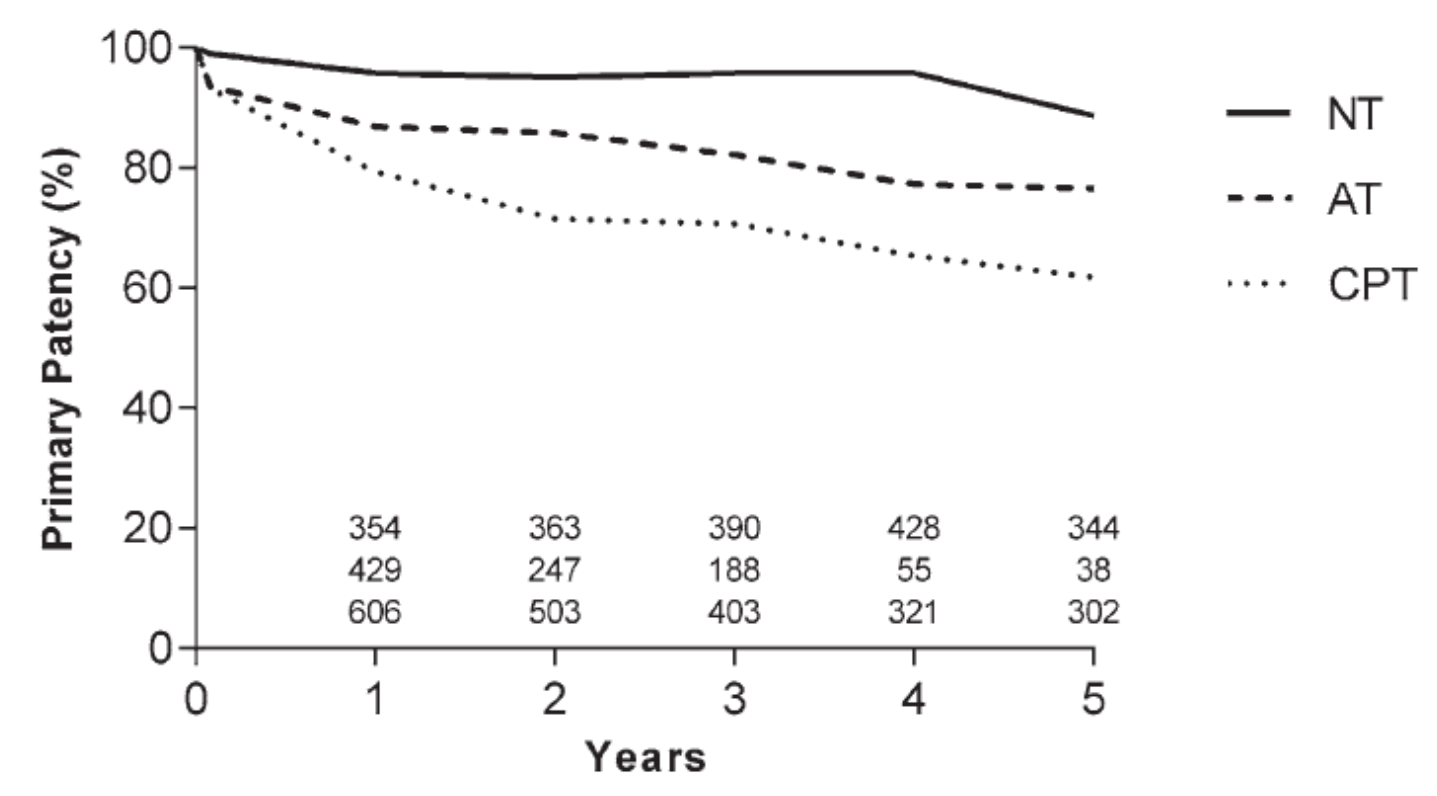
Venous Stenting: Results in Lower Extremities



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

Razavi MK, et al. Circ Cardiovasc Interv. 2015;8(10):e002772.

Safety

- 98.8% freedom from MAEs through 30 days
  - Lower confidence limit of 95.8% exceeded the performance goal of 94%

Major Adverse Events (through 30 days)	n/N
Arterial or venous injury at the target vessel segment and/or target lesion location or at the access site requiring surgical or endovascular intervention	2/169 (1.2%)
Device or procedure-related death	0/169
Bleeding at the target vessel and/or target lesion or at the access site requiring surgical or endovascular intervention or blood transfusion	0/169
Acute DVT outside the target vein segment	0/169
Clinically significant pulmonary embolism	0/169
Embolization of the stent	0/169

MAEs were adjudicated by a Clinical Events Committee.

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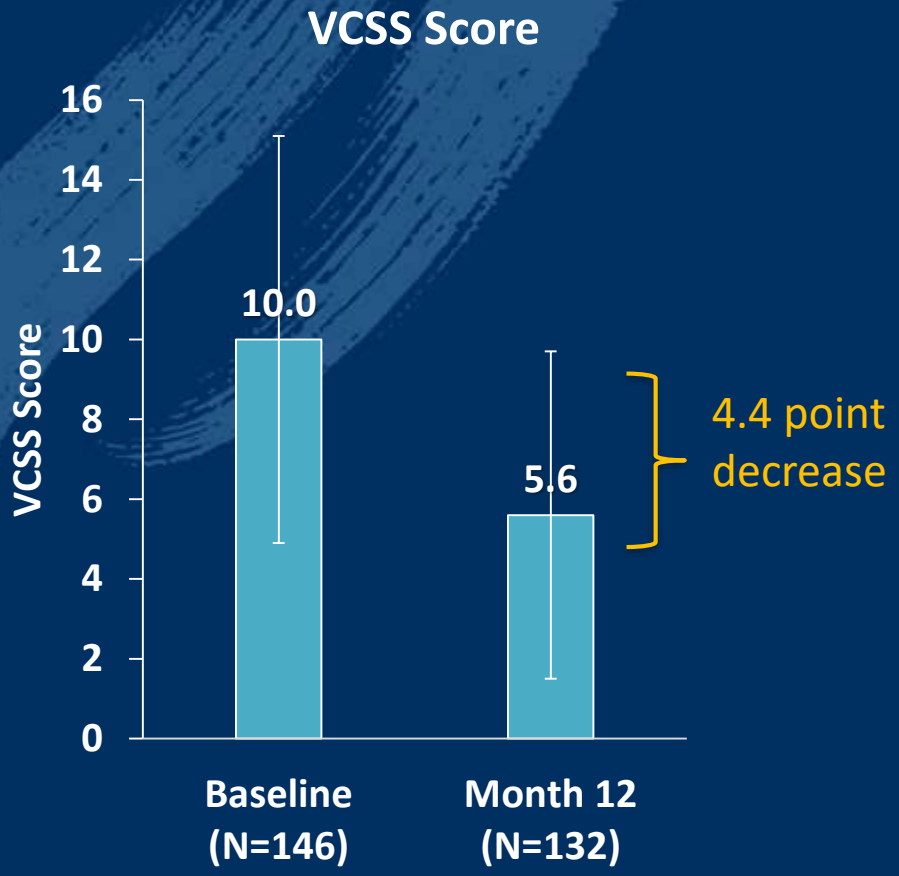
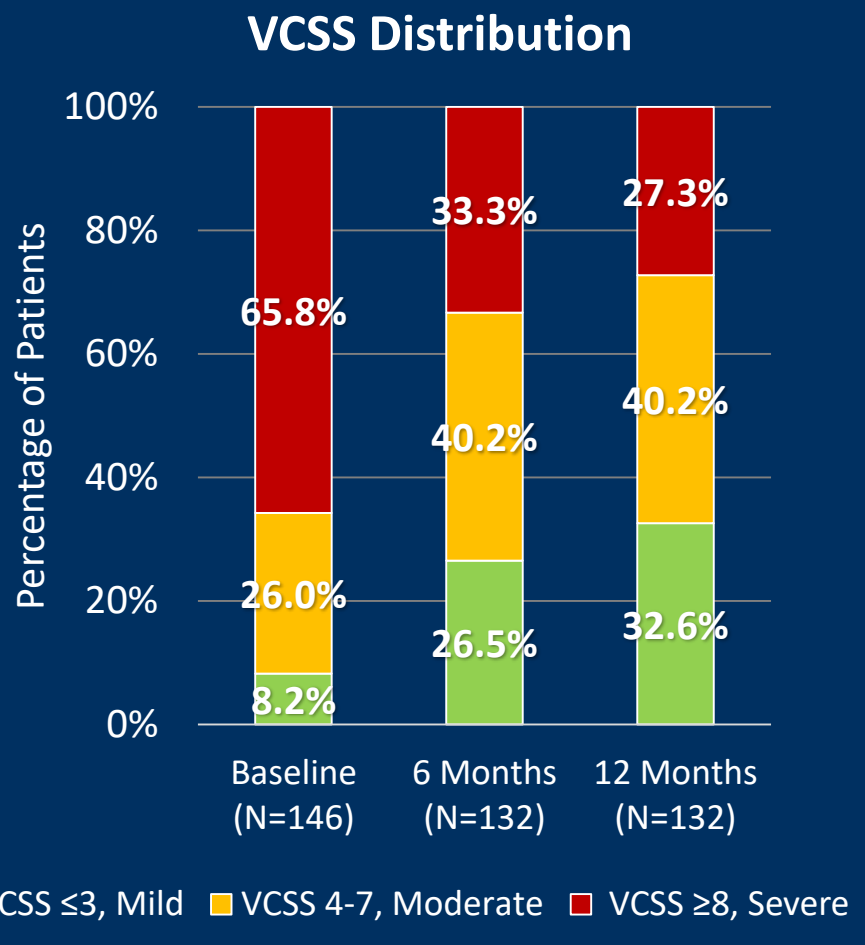
Clinical Severity





VIRTUS

Conclusions

- VIRTUS primary safety and effectiveness endpoints successfully met
- Patient sample with challenging characteristics:
  - 75% Post-thrombotic
  - ~25% “C” 5-6
  - 31% with occlusion
  - 32% had involvement of the entire iliofemoral segment
- 84% 12-month primary patency for patients treated with the VICI stent
- The VICI Venous stent demonstrated excellent safety outcomes with 98.8% freedom from MAE through 30 days

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