

IVUS Guided Treatment of Deep Vein Occlusive Disease to Heal Venous Ulcers: The IGuideU Trial

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Disclosure

Speaker name:

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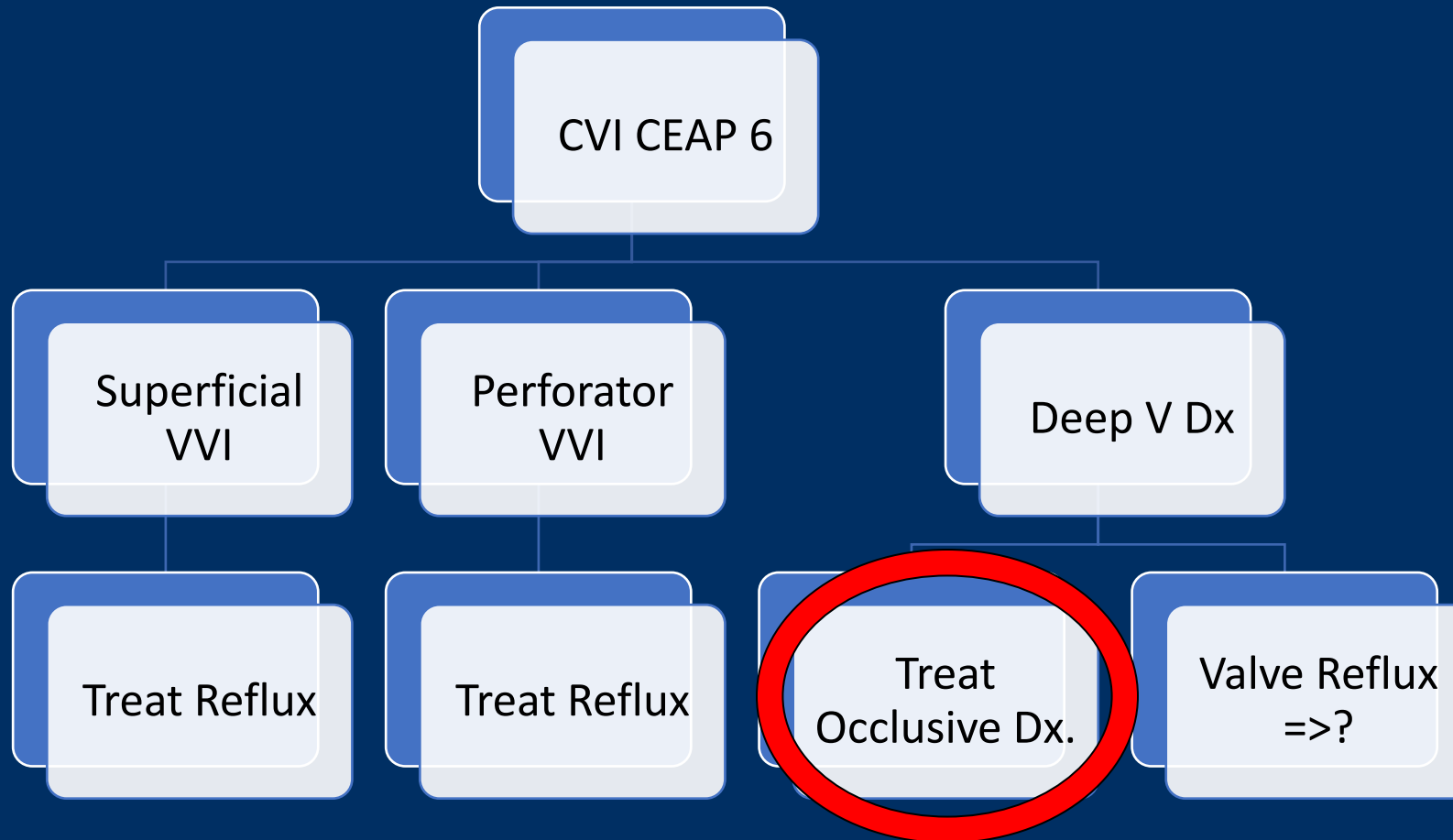
I have the following potential conflicts of interest to report:

- 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



CVI in Patient with Venous Leg Ulcer (VLU)

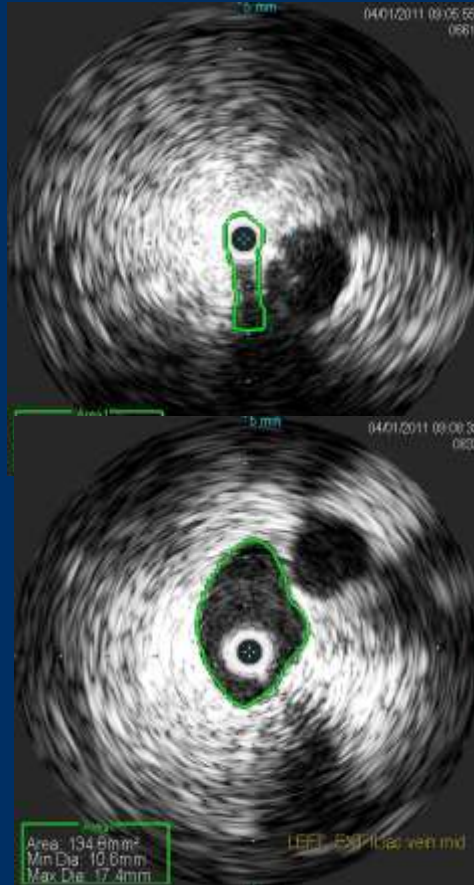


IVUS EIV => 70% CSA Stenosis

18 mos.
Duration / Treatment



EIV stenosis



9 months post EIV stent



Incidence of and risk factors for ilio caval venous obstruction (ICVO) in patients with active or healed VLU

- 78 cCEAP 5 / 6 patients
- evaluated w/ CT or MR venogram
- 37% => 50% iliac vein stenosis
- 23% => >80% iliac vein stenosis

Advanced CVI / Iliofemoral Vein Occlusive Disease

Journal of
Vascular Surgery®

J Vasc Surg 2006;44

- N=332 limbs stented
- Non thrombotic stenosis
- Complete ulcer healing
- 76% pts. after IVUS guided stent

High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: A permissive role in pathogenicity

Seshadri Raju, MD, and Peter Neglen, MD, PhD, *Floresed, Alir*

Purpose: Nonthrombotic iliac vein lesions (NIVL), such as webs and spurs described by May and Thurman, are commonly found in the asymptomatic general population. However, the clinical syndrome, variously known as May-Thurman syndrome, Cockett syndrome, or iliac vein compression syndrome, is thought to be a relatively rare contributor of chronic venous disease (CVD), predominantly affecting the left lower extremity of young women. The present study describes the much broader disease profile that has emerged with the use of intravascular ultrasound (IVUS) scanning for diagnosis and analyses stent placement outcome in two specific NIVL subsets that may offer clues to their pathogenic role.

Methods: Among 4026 patients with CVD symptoms spanning the range of CEAP clinical classes, IVUS examinations were selectively done in severely symptomatic patients for indications as described. Iliac vein obstructive lesions were found in 938 limbs of 879 patients; 53% of the limbs had NIVL, 40% were post-thrombotic, and 7% were a combination. Stents were placed in 332 limbs in 319 patients in two NIVL subsets. The subsets, one with and one without associated distal limb reflux, were compared. Reflux was left untreated in the first subset.

Results: The median age was 54 years (range, 18 to 90 years). The female-male ratio was 6:1 and the left-right ratio was 3:1. NIVL lesions in the iliac vein occurred at the iliac artery crossing (proximal lesion) and also at the hypogastric artery crossing (distal lesion), a new IVUS finding. Venography was only 66% sensitive, with 34% of venograms appearing "normal." IVUS had a diagnostic sensitivity of >90%. The cumulative results observed at 2.5 years after stent placement in the NIVL subsets with reflux and without reflux, respectively, were complete relief of pain 82% and 77%, complete relief of swelling 47% and 53%, complete stasis ulcer healing 67% and 76%, and overall clinical relief outcome 78% and 79%. These results are nearly identical between the two subsets even though distal reflux remained uncorrected in the NIVL plus reflux subset.

Conclusions: NIVL has high prevalence and a broad demographic spectrum in patients with CVD. Similar lesions in the asymptomatic general population may be permissive of future development of CVD. Stent placement alone, without correction of associated reflux, often provides relief. (J Vasc Surg 2006;44:136-44.)

Virchow¹ attributed the increased left-sided predilection of deep venous thrombosis to left iliac vein compression by the crossing artery. In 1908, McMurrich² first reported the presence of web-like intrinsic intraluminal lesions in 53% of 107 unselected cadavers. Subsequent large autopsy series³⁻⁵ confirmed the surprisingly high prevalence of the lesion in the asymptomatic general population. There is disagreement if the lesions are ontogenic at embryonic venous fusion sites⁶ or traumatic from the pulsations of the overlying artery. A post-thrombotic etiology appears to be ruled out,^{4,5} even though instances of secondary thrombosis apparently induced by the lesions are well documented.^{7,8}

Corrosion cast and venographic studies suggest that the incidence of extrinsic compressive lesions may be even more pervasive than intrinsic lesions.^{9,7} Recent imaging data⁹ indicate that compression of the left iliac vein at the arterial crossover point may be present in 66% of the general population without any venous symptoms. Because imag-

ing methods, including intravascular ultrasound (IVUS), cannot differentiate intrinsic from extrinsic lesions with sufficient clarity, the generic term *nonthrombotic iliac vein lesions* (NIVL) is used throughout this report to be inclusive of both types of lesions.

Despite the widespread prevalence of the lesion in the general population, the clinical syndrome (iliac vein compression syndrome, May-Thurman syndrome, or Cockett syndrome) is thought to be a relatively rare cause of chronic venous disease (CVD), responsible for only 1% to 5% of cases.¹⁰ The diagnosis is often established by venography in selected cases fitting the classic clinical profile described by Cockett and Thomas¹¹ of severe left limb symptoms of pain and swelling in young women. The diagnostic sensitivity of venography for nonthrombotic iliac vein type lesions is known to be poor.⁹ Liberal use of the more sensitive IVUS^{11,12} yields a more diverse picture of the syndrome than previously appreciated; particularly, we found the incidence of nonthrombotic iliac vein type lesions to be very high in symptomatic CVD cases. The question then arises if these lesions are pathogenic in CVD or simply incidental findings. Outcome data after successful stent correction of the lesions in two specific subsets described below suggests that NIVLs may play a permissive role in the development of CVD.

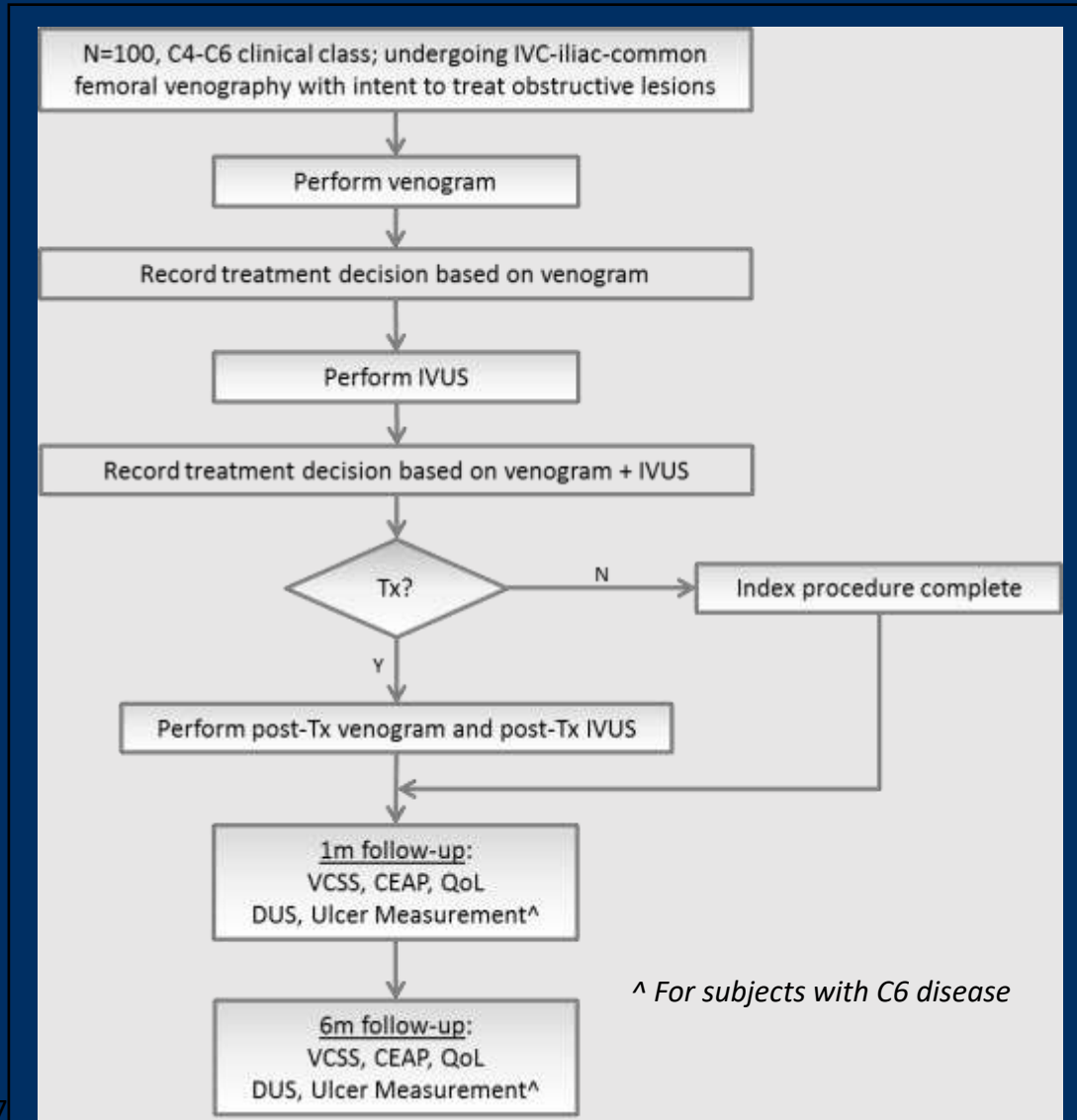
From the University of Mississippi Medical Center and River Oaks Hospital, Compression of arteries: none.

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VIDIO Trial: Study Design



- Prospective, multi-center, single-arm
- 14 Sites: US (n = 11) and Europe (n = 3)
- 100 patients
 CEAP 4-5, n=50; CEAP 6, n=50
- Follow-up visits: 1m and 6m



Ulcer Size: IVUS Guided Stents Stented / SOC vs. Non-stented (SOC)

Time Point	Mean in Stented Subjects (N = 36)	Mean in Non-Stented Subjects (N=14)
Subjects	36 (72%)	14 (28%)
Baseline	34.6 cm ²	20.5 cm ²
1 month	26.0 cm ²	12.2 cm ²
6 months	27.5 cm ²	18.4 cm ²
Baseline vs. 1 month	P = .002	P = .021
Baseline vs. 6 months	P = .017	P = .055
1 Month vs. 6 months	P = .855	P = .202

Wilcoxon Signed Ranks Test

Conclusion: Literature Review

- IVUS guided treatment of Iliofemoral V. occlusive dx. can promote VLU healing
- Prospective study v. SOC needed

IGuideU Trial

Global Principal Investigators

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IGuideU: Study Objectives:

- **Primary Objective:**

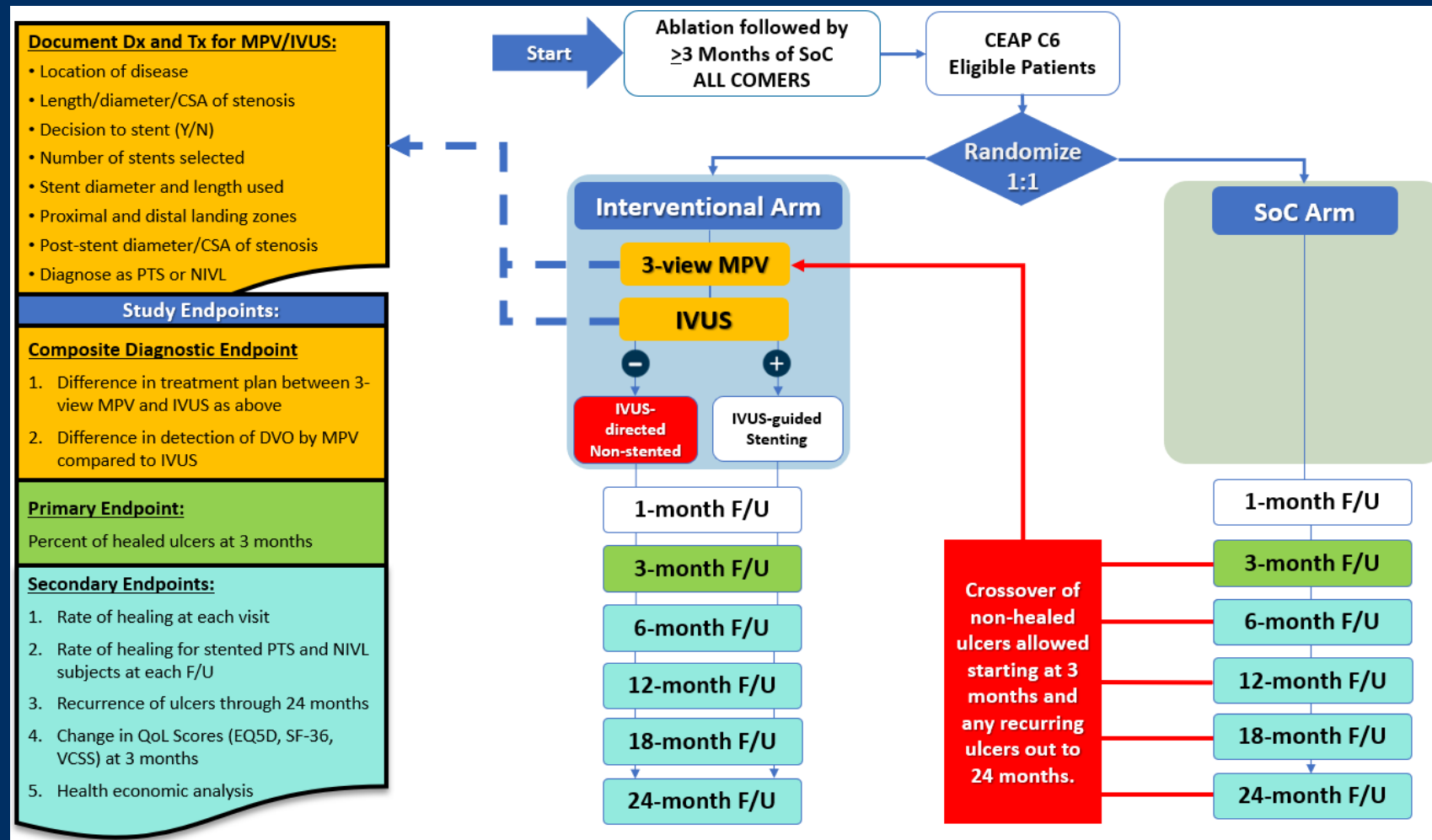
Determine if the diagnosis of CIV / EIV / CFV venous obstruction (DVO)

- Intravascular ultrasound (IVUS)
- Subsequent IVUS guided endovascular intervention
- Improves Venous Leg Ulcer (VLU) healing vs. standard of care (SoC)

- **Secondary Objectives:**

- Diagnostic: assess change in DVO treatment decisions between MPV and IVUS imaging information
- Long-term clinical outcomes: assess time to VLU healing/ulcer recurrence
- Economic Analysis: compare cost of IVUS-guided interventional treatment in healing of VLUs compared to SoC.

IGuideU: Study Schematic



IGuideU: Study Objectives:

- Global, prospective, multi-center, randomized controlled trial
 - US, UK, France, Germany, Australia
- Total of up to 250 subjects, up to 30 sites, with 24-month follow-up
- Primary Clinical Endpoint: Percent of healed ulcers between groups at 3 months
- Philips IVUS imaging with Visions PV 0.035



IGuideU: SOC Arm Treatment Guidelines “Highlights”

Mandate

- Compression therapy/dressing

• Allow

- Periodic leg elevation.
- Sclerotherapy under ulcer bed.
- Mechanical debridement as needed.
- Systemic antibiotics if diagnosed with infection
- Pain management (Pentoxifylline/Trental) allowed
- Topical antimicrobial as needed.

Prohibited

- Negative pressure systems.
- Artificial and/or autologous skin grafting within first 3 months after randomization / Crossover
- Skin substitutes and tissue-based therapies within first 3 months after randomization / crossover
- Growth factors within first 3 months after randomization / crossover
- Experimental topical creams and lotions.

IGuideU: Schedule of Assessments

- 2 Year Follow-Up:
- Wound Care
- Duplex US
- CEAP / VCSS / SF-36 / EQ5D

	Screening Visit	Baseline Visit	1 Month (30 days)	3 Months (90 days)	6 Months (180 days)	12 Months (365 days)	18 Months (545 days)	24 Months (720 days)	Early Termination Visit*	Unscheduled Visit*	Re-intervention Procedure*
Visit Window	-30 to 0 days	NA	±14 days	±14 days	±30 days	±30 days	±30 days	±30 days	NA	NA	NA
Visit Type	Office	Hospital/OBL	Office	Office	Office	Office	Phone Call	Phone Call	Office/Hospital/OBL	Office/Hospital/OBL	Hospital/OBL
Informed Consent	X										
Medical History	X										
Eligibility/Inclusion and Exclusion Criteria	X										
Urine Pregnancy Test ^a	X	X									X
Enrollment and Randomization	X										
Duplex Ultrasound ^b	X		X	X	X	X					
Physical examination	X		X	X	X	X				X	X
Anticoagulant and Antiplatelet	X	X	X	X	X	X	X	X		X	X
Clinical Laboratory Tests ^{c, d, e}	X										
Venous Ulcer Assessment	X	X	X	X	X	X				X	X
CEAP Clinical Category	X	X	X	X	X	X			X	X	X
VCSS Category	X	X	X	X	X	X			X	X	X
Subject Diary Review ^f		X	X	X	X	X	X	X	X	X	X
Wound Care Management Education ^g		X	X	X	X	X					X
SF-36		X	X	X	X	X	X	X	X	X	X
EQ5D Questionnaire		X	X	X	X	X	X	X	X	X	X
MPV Imaging		X									X
IVUS Imaging		X									X
Adverse Events ^h		X									X
Patient-completed Diary	Completed monthly for study duration, through 24 months										

IGuideU Trial

Plan for First Patient Enrollment
1st Quarter of 2021



Thank You!