VEITH SYMPOSIUM Connecting The Vascular Community

VANDERBILT School of Medicine

Update on The PROMISE Trials Results in No Option CLTI Patients

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on Behalf of PROMISE I, II, UK, and CLariTI Investigators

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CONFLICTS

- Consultant: BSCI, Perdix, Inari/LimFlow, Elastimed, Medtronic, Shockwave, Caeli Med, BD

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CLTI: The most severe form of peripheral arterial disease

3.8M — In the U.S. **affected by Chronic Limb-Threatening Ischemia** (CLTI) and the number continues to grow[1]

150K — **Major lower extremity amputations** in the U.S. annually[2]

4X — **More likely to face major amputation** if you are Black[3]

6th — **Most expensive surgical procedure** in the U.S. = Major Amputation[4]

Driven by high complication rates, length of stay, readmissions, and hospitalizations[4]

1. Nehler M.R., Duval S., Diao L., Annex B.H., Hiatt W.R., Rogers K., Zakharyan A., Hirsch A.T. Epidemiology of peripheral arterial disease and critical limb ischemia in an insured national population. J. Vasc. Surg.
2. Creager et al. Reducing Nontraumatic Lower-Extremity Amputations by 20% by 2030: Time to Get to Our Feet: A Policy Statement From the American Heart Association. Circulation 2021
3. https://diabetes.org/get-involved/advocacy/amputation-prevention-alliance Accessed on September 6th, 2023
4. Yost ML. Cost-Benefit Analysis of Critical Limb Ischemia in the Era of the Affordable Care Act. 2014. Endovascular Today.

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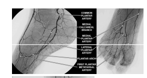
CLTI: The most severe form of peripheral arterial disease

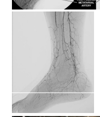
20%
of CLTI patients become "no-option"[1]

>50%
of no-option patients die or require major amputation within 6 months[2]

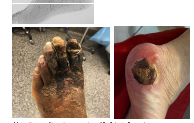
NORMAL FOOT



SEVERE ISCHEMIA
No acceptable **arterial** target for standard revascularization



CHRONIC WOUNDS
Typically do not heal without successful reperfusion



Maturation surveillance images courtesy of Dr. Roberto Ferraresi

1. Kum S, Tan YK, Schreve MA, Ferraresi R, Varcoe RL, Schmidt A, et al. Midterm outcomes from a pilot study of percutaneous deep vein arterialization for the treatment of no-option critical limb ischemia. J Endovasc Ther 2019;24:619-26.
2. Ghare MI MCP, BA; Daniela Tirziu, PhD; Helen Parise, ScD; Roseann White, PhD; S. Elissa Altin, MD; Sameer Nagpal, MD; Alexandra Lansky, MD. Chronic Critical Limb Ischemia With

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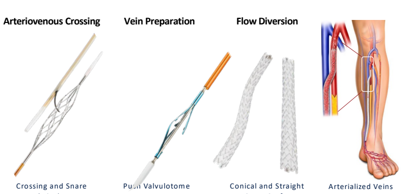
TADV with the LimFlow System



LimFlow System Highlights

- **Physician Specialties:** Vascular surgery & interventional radiology / cardiology
- **Site of Service:** Primarily hospital-based peripheral interventions
- **Only On-Label Device for No-Option CLTI**
  - FDA PMA approved 2023
  - Original CE-mark 2016

INDICATIONS FOR USE: indicated for patients who have been diagnosed with chronic limb-threatening ischemia and have no suitable endovascular or surgical options. **Caution**: This device is restricted for sale by or on the order of a physician. All trademarks are property of their respective owners.

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The Mounting Evidence

Multicenter | Prospective | Independent Review Committee for Eligibility

	PROMISE I	PROMISE UK	PROMISE II	PROMISE III	CLariTI
	Early feasibility study	UK study	US pivotal study	Post-market study	Natural progression of high-risk CLTI
Inc Criteria	Rutherford 5/6 No-option CLTI	Rutherford 5/6 No-option CLTI	Rutherford 5/6 No-option CLTI	Rutherford 5/6 No-option CLTI	Rutherford 5/6 No-option CLTI or multiple failed revascularizations
Enrollment	Complete	Complete	Follow-up ongoing	Ongoing	Complete
# of Centers	7	9	20	25	30
# of Patients	32	28	105	100	180
1° Endpoint	AFS at 6 mos.	AFS at 12 mos.	AFS at 6 mos.	AFS at 6 mos.	AFS at 12 mos.

Data in perspective

Baseline Characteristics

PROMISE I, II and UK versus CLariTI

	PROMISE I N=32	PROMISE UK N=24	PROMISE II N=81	All patients N=137
Age	**72.0** (59.5-82.5)	**68.5** (60.5-74.0)	**71.0** (65.0-76.0)	**71.0** (63.0-77.0)
Male sex – no. (%)	**21** (65.6%)	**22** (91.7%)	**57** (70.4%)	**100** (73.0%)
BMI, kg/m²	**25.6** (23.4-28.9)	**25.1** (22.9-28.1)	**25.4** (22.3-28.2)	**25.3** (22.6-28.4)
Rutherford classification				
Stage 5	**28** (87.5%)	**23** (95.8%)	**53** (65.4%)	**104** (75.9%)
Stage 6	**4** (12.5%)	**1** (4.2%)	**28** (34.6%)	**33** (24.1%)
Prior intervention in target limb	**25** (78.1%)	**22** (91.7%)	**60** (74.1%)	**107** (78.1%)
Smoking	**22** (68.8%)	**20** (83.3%)	**36** (44.4%)	**78** (56.9%)
Diabetes mellitus	**22** (68.8%)	**20** (83.3%)	**63** (77.8%)	**105** (76.6%)
Chronic kidney disease[a]	**11** (34.4%)	**2** (8.3%)	**20** (24.7%)	**33** (24.1%)

[a]Chronic kidney disease (CKD) was defined as either serum creatinine >2.5 mL/dl or eGFR >30ml/min.

Data in perspective

Clinical Outcomes

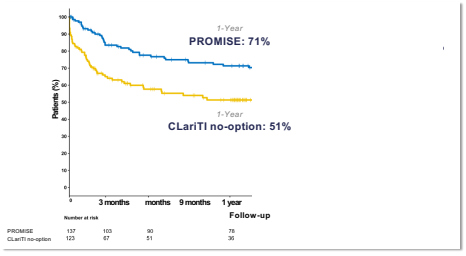
PROMISE I, II and UK versus CLariTI

	PROMISE Studies[1] Patient-level pooled data	CLariTI Registry[2] Natural history of no-option CLTI
Study type	Prospective	Prospective
Enrollment	Complete	Complete
# Patients	**165**	122
Countries	US and UK	US
Independent adjudication of no-option	Yes	Yes
Outcomes		
Technical success	99%	-
Wounds healed/healing – 6M/12M	80% / 83%	NR
Amputation-free survival – 6M/12M	74% / 66%	38% / 33%
Limb salvage – 6M/12M	80% / 74%	52% / 48%

Long-term outcomes

Limb Salvage Durable to 2 Years

PROMISE I and PROMISE II



Long-term outcomes

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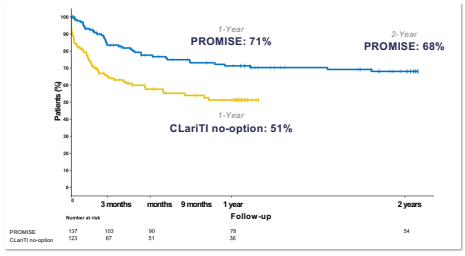
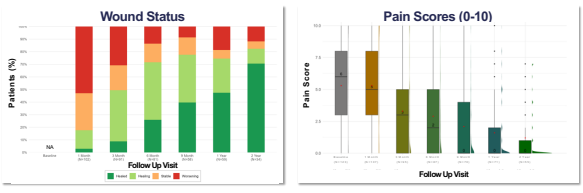


Long-term outcomes

Wound Status and Pain Scores at 2 Years

PROMISE I and PROMISE II



Propensity score matching

Study Design

No-option CLTI
Rutherford 5/6 – non-healing ischemic ulcers and gangrene

TADV
- LimFlow is the only FDA-approved device for TADV
- PROMISE I, II, and UK trials

Non-TADV
- Natural history of patients not treated with TADV
  - Lack of target
  - Multiple failed revascularization attempts
  - Off-label deep vein arterialization
- CLariTI registry

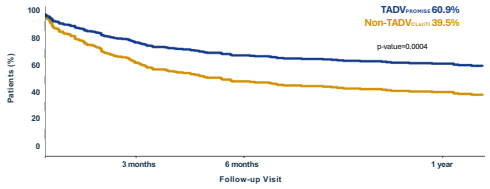
Objective: Compare clinical outcomes and cost-effectiveness in TADV patients versus non-TADV patients

Powell AI, et al. Featured Clinical Research. TCT 2024.

Propensity score matching

1 Year AFS K-M Rate | Matched Population

N=278

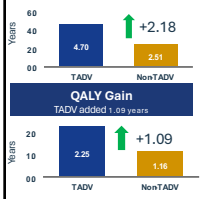


Powell Kr et al. Featured Clinical Research. TCT 2024
Survival probabilities and p-values derived from Cox proportional hazards

Cost-effectiveness analyses

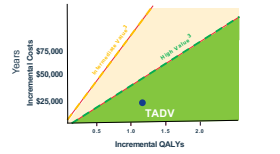
TADV with LimFlow is Highly Cost-effective

Survival Gain
TADV added 2.18 years



QALY Gain
TADV added 1.09 years

Incremental Lifetime Cost-Effectiveness
$21,694 per QALY gained $33,647 with full NTAP



Powell Kr et al. Featured Clinical Research. TCT 2024
ICER: incremental cost-effectiveness ratio; NTAP: new technology add-on payment; QALY: quality adjusted life years; TADV: transcatheter arterialization of deep veins; TAVR: transcatheter aortic valve replacement; TMVr: transcatheter mitral valve repair;

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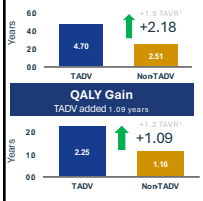

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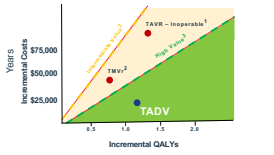

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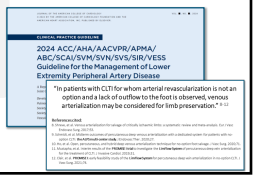
Conclusions

- **Only** FDA approved device for TADV
- Procedure **reproducible and generalizable**
- TADV intervention is **high-value and cost-effective** due to the substantial clinical improvements inherent to the LimFlow procedure
- LimFlow **mentioned by name** in the 2024 Guidelines[1]
- PROMISE III currently enrolling

Benefit with TADV	
AFS	+21.4%
Survival	+2.2 yrs
QALYs	+1.1 yrs



[1]Gornik HL, et al. J Am Coll Cardiol. 2024;83:2497-2604.