PROMISE II Trial and CLariTI Analysis

Peter A. Schneider, MD
University of California San Francisco
Disclosure

Speaker name: Peter A. Schneider

I have the following potential conflicts of interest to report:

- Consulting: Boston Scientific, Surmodics, Silk Road, Medtronic, Cagent, LimFlow, Acotec, Abbott (DSMB)
Major amputations in the US and CLariTI Sites

CLariTI Registry:
- 180 patients at 22 sites participated, mix of academic centers and community hospitals
  - Vascular Surgeons
  - Interventional Cardiologists
  - A. Dua, MD PI

Inclusion:
- Rutherford 5/6 CLTI

No-Option
- No option for conventional endovascular or surgical intervention
- No-option status determined by treating physician

Multiple Revasc Fails
- 2+ revascularization attempts in previous 6 months without resolution of symptoms

Exclusion:
- Subject participating in the PROMISE II Clinical Trial of TADV

### CLariTI Baseline Clinical Characteristics (n=180)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range)</td>
<td>70 (60-78)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>120 (66.6%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>99 (55.0%)</td>
<td></td>
</tr>
<tr>
<td>Black or African Descent</td>
<td>65 (36.1%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>4 (2.2%)</td>
<td></td>
</tr>
<tr>
<td>Unknown/Declined to State</td>
<td>11 (6.1%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>156 (86.7%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>19 (10.6%)</td>
<td></td>
</tr>
<tr>
<td>Unknown/Declined to State</td>
<td>5 (2.8%)</td>
<td></td>
</tr>
<tr>
<td>History of Smoking</td>
<td>108 (60.0%)</td>
<td></td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Failure</td>
<td>59 (32.8%)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>141 (78.3%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>166 (92.2%)</td>
<td></td>
</tr>
</tbody>
</table>

### Diabetes
- Type I: 4%
- Type II: 71%
- Not Diabetic: 25%

### Renal Disease
- None: 49%
- CKD: 23%
- ESRD: 25%
- RI: 3%
### CLariTI 6-Month Interim Results

#### Median Age (range)
- Median Age: 70 (60-78)

#### Male
- Male: 120 (66.6%)

#### Race
- Caucasian: 99 (55.0%)
- Black or African Descent: 65 (36.1%)
- Asian: 4 (2.2%)
- Unknown/Declined to State: 11 (6.1%)

#### Ethnicity
- Not Hispanic or Latino: 156 (86.7%)
- Hispanic or Latino: 19 (10.6%)

#### No-Option/Desert Foot (n=121)
- AFS Rate: 38%

#### Multiple Revasc Fails (n=59)
- 2+ Revasc Fails: 48%

#### Full Cohort (n=180)
- No Option: 66%
- 2+ Revasc Fails: 34%
PROMISE II Overview

**US Pivotal Trial**
Multicenter, prospective pivotal study of the LimFlow System

**KEY CRITERIA**

**Inclusion**
- No-Option CLTI
- Rutherford 5/6
- Stable Dialysis allowed

**Exclusion**
- Life expectancy <12M
- Severe heart failure
- Hepatic Insufficiency

**ENROLLMENT**
- 105 patients
- 20 sites in US

**NATIONAL PIs**
- Dr. Dan Clair
  Vanderbilt University
- Dr. Mehdi Shishehbor
  University Hosp. Cleveland

**PRIMARY ENDPOINT**
Bayesian

**SECONDARY ENDPOINT**
Amputation Free Survival (AFS) at 6M

- Pre-specified literature-based PG of 54%

- Technical Success
- Wound Healing
- Rutherford Class
- Pain
LimFlow TADV System

Transcatheter Arterialization of Deep Veins (TADV)

► Leverage healthier veins as a conduit
► Create new routes to perfuse tissue
► Integrated system for AV Crossing, atraumatic vein preparation and flow focalization

CAUTION: Investigational device. Limited by Federal law to investigational use.
PROMISE II Participating Centers

United States, Puerto Rico

- Baylor
- San Lucas Hospital
- Dartmouth-Hitchcock
- Mass Gen
- Coastal Vascular Institute
- UH Cleveland
- St Luke's
- Cardiac and Vascular Institute
- Atrium Health
- Boston Medical Center
- Harbor-UCLA
- Ochsner
- Prisma Health
- UnityPoint
- UCSF
- Seton Ascension Austin
- Vanderbilt
- Yale
- Presbyterian
- University of Florida

- Montero-Baker, Mills
- Martinez-Trabal
- Powell
- Dua
- Weatherford
- Shishehbor
- Bunte
- Lee
- Stanley
- Farber
- Archie, Kansal, Bowens
- N'Dandu
- Virvilis, Gray
- Scott
- Conte, Vartanian, Schneider
- Ferrer
- Clair, Stone
- Chaar, Cardella
- Henao
- Jacobs
## PROMISE II Patient Demographics

### BASELINE CHARACTERISTICS (n=105)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Avg, years)</td>
<td><strong>69</strong> (38-89)</td>
</tr>
<tr>
<td>Gender (% Male)</td>
<td><strong>69%</strong></td>
</tr>
<tr>
<td>African American</td>
<td><strong>15%</strong></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td><strong>28%</strong></td>
</tr>
</tbody>
</table>

### COMORBIDITIES

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td><strong>77%</strong></td>
</tr>
<tr>
<td>Hypertension</td>
<td><strong>91%</strong></td>
</tr>
<tr>
<td>Dialysis</td>
<td><strong>18%</strong></td>
</tr>
<tr>
<td>CKD</td>
<td><strong>39%</strong></td>
</tr>
<tr>
<td>Rutherford 5</td>
<td><strong>65%</strong></td>
</tr>
<tr>
<td>Rutherford 6</td>
<td><strong>35%</strong></td>
</tr>
</tbody>
</table>

### PROCEDURAL RESULTS

- **Technical Success**: **99%**

### Crossing Artery

- **PTA**: 6%
- **Peroneal**: 19%
- **TPT**: 75%

Data on file LimFlow
Patient Demographics

- 72-year-old male, R5 CLTI
- Type II diabetes, hypertension, severely calcified peripheral arteries, and contralateral amputation due to CLTI.
- Ulcers present for 24 months.
- Toe-brachial index (TBI) was 0.24 at baseline, 0.64 at 6 months, 0.89 at 12-months, and 0.61 at 24-months (normal TBI is greater than 0.65).

Image Legend

A-D) Baseline angiograms
E) Angiogram after establishing the TADV circuit
F, G) Angiographic imaging at 24 months
H-J) Panels showing the progression of wound healing after TADV
PROMISE II Primary Endpoint
6 Month AFS, Limb Salvage, Survival

6 Month Data
Survival = 87%
Limb Salvage = 76%
AFS = 66%

Data on file LimFlow
PROMISE II met its performance goal including all sensitivity analyses.

180-Day Amputation-Free Survival Rate

Posterior Mean
0.66
95% BCI: (0.565, 0.745)

Probability that trial exceeds pre-specified performance goal of 54% = 0.9931.

Needed > 0.977 to win

PROMISE II Primary Endpoint
6 Month AFS – Per Protocol (Bayesian)

Probability Density

Inferior
Superior

0.0 0.2 0.4 0.6 0.8 1.0

Probability Density 0.54 PG

180-Day Amputation-Free Survival Rate

Data on file LimFlow
PROMISE II Wound Core Lab Results—Healing Status

Follow-up Timepoint (MOS)

Data on file LimFlow
PROMISE II and CLariTI Conclusions

CLariTI
- Provides a much needed data set of real-world outcomes
- CLariTI Outcomes in no-option patients
  - 47% major amputation
  - 38% amputation free survival in no option patients
- Imminent need for new therapies in this understudied population

PROMISE II
- 76% limb salvage in no-option patients
- 66% Amputation free survival
- PROMISE II pivotal trial met its primary endpoint