Dissection repair BTK: evidence review from TOBA II BTK

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Disclosure

Speaker name:
Dr. Michael Lichtenberg

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
Chronic Limb-Threatening Ischemia (CLTI)

- Afflicts 2-3.4 million people in the US\(^1\)

- Treatment of BTK arteries for CLTI remains based on angioplasty
  - Dissection is frequent and is a predictor for restenosis\(^2\)

\(^1\)Yost, The SAGE Group 2016
\(^2\)Schillinger, Radiology 2002
Tack Endovascular System (4F)

Multi-implant, minimal-metal focal dissection repair for tapering vessels from knee to ankle

Tack® Implants

• Four pre-loaded nitinol implants
• 6mm deployed length
• Each implant self-sizes to tapering BTK anatomy
  • 1.5 – 4.5mm RVD

OTW Delivery System

• 4F / .014”
• 150cm working length
• Accurate (≤1mm) deployment

INTENDED USE: The Tack Endovascular System (4F, 1.5-4.5mm) is intended for use in mid/distal popliteal, tibial and peroneal arteries, ranging in diameter from 1.5 mm to 4.5 mm, for the repair of post percutaneous transluminal balloon angioplasty (PTA) dissection(s).

CONTRAINDICATIONS: The Tack Endovascular System is contraindicated for the following: 1. Patients with residual stenosis in the treated segment equal to or greater than 30% after PTA. 2. Tortuous vascular anatomy significant enough to prevent safe introduction and passage of the device. 3. Patients with a known hypersensitivity to nickel-titanium alloy (Nitinol). 4. Patients unable to receive standard medication used for interventional procedures such as anticoagulants, contrast agents and antiplatelet therapy.

The Tack Endovascular System is CE Mark authorized under EC Directive 93/42/EEC. Tack Endovascular System® and Tack® are registered trademarks of Intact Vascular, Inc.
Study Design and Follow-Up

**Prospective, single-arm pivotal IDE study**

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients with CLI and angiographic evidence of a dissection post-PTA requiring repair in the mid/distal popliteal, tibial and/or peroneal arteries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment</td>
<td>233 patients at 41 US, international sites</td>
</tr>
</tbody>
</table>
| Primary Endpoints | • Safety: MALE + POD at 30d  
• Efficacy: freedom from MALE at 6m + POD at 30d |  |
| Secondary Endpoints | • Tacked segment patency at 6 months (DUS flow/no flow)  
• Target limb salvage at 6 months |  |
| Key Observational Endpoints | • Dissection resolution  
• Freedom from CD-TLR  
• Target lesion patency  
• Amputation-free survival  
• Changes from baseline:  
  - Rutherford  
  - Wound status  
  - Quality of life |  |

**Enrollment (n=233)**

1-M Follow-up (n=220)
- 12 missed visit
- 1 terminated study prior to visit

6-M Follow-up (n=199)
- 19 missed visit
- 15 terminated study prior to visit

12-M Follow-up (n=180)
- 24 missed visit
- 29 terminated study prior to visit

MALE + POD: composite of all-cause death, above-ankle target limb amputation, or major re-intervention to the target lesion(s), defined as new bypass graft, jump/interposition graft revision, or thrombectomy/thrombolysis.
## TOBA II BTK Investigators

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Matthews, NC  

Neil Strickman  
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David Dexter  
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### Angiographic Core Lab / Clinical Events Committee: Yale Cardiovascular Research Group (New Haven, CT)  
### Duplex Ultrasound Core Lab: VasCore (Boston, MA)
### Baseline Patient/Lesion Characteristics

#### Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD (N) or % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>74.4 ± 10.0 (233)</td>
</tr>
<tr>
<td>Male Gender</td>
<td>67.4% (157/233)</td>
</tr>
<tr>
<td><strong>Rutherford</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>16.3% (38/233)</td>
</tr>
<tr>
<td>4</td>
<td>33.5% (78/233)</td>
</tr>
<tr>
<td>5</td>
<td>50.2% (117/233)</td>
</tr>
<tr>
<td>TBI target limb</td>
<td>0.43 ± 0.23 (118)</td>
</tr>
<tr>
<td>Smoking History</td>
<td>62.2% (145/233)</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td>65.7% (153/233)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>93.6% (218/233)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>56.1% (129/230)</td>
</tr>
<tr>
<td>MI</td>
<td>22.0% (51/232)</td>
</tr>
<tr>
<td>PCI / CABG</td>
<td>43.9% (101/230)</td>
</tr>
<tr>
<td><strong>Chronic renal insufficiency</strong></td>
<td>24.6% (57/232)</td>
</tr>
</tbody>
</table>

#### Lesion Characteristics (core lab adjudicated)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD (N) or % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RVD (mm)</strong>*</td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>3.5 ± 1.0 (248)</td>
</tr>
<tr>
<td>Distal</td>
<td>2.6 ± 0.7 (248)</td>
</tr>
<tr>
<td><strong>Lesion length (mm)</strong>†</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>80 ± 49 (248)</td>
</tr>
<tr>
<td><strong>PTA Treatment</strong></td>
<td>154 ± 110 (238)</td>
</tr>
<tr>
<td><strong>Pre-PTA DS%</strong></td>
<td>85 ± 17 (248)</td>
</tr>
<tr>
<td><strong>Total Occlusion</strong></td>
<td>47.6% (118/248)</td>
</tr>
<tr>
<td><strong>Calcium (PARC)</strong></td>
<td></td>
</tr>
<tr>
<td>None/mild</td>
<td>64.1% (159/248)</td>
</tr>
<tr>
<td>Moderate</td>
<td>18.1% (45/248)</td>
</tr>
<tr>
<td>Severe</td>
<td>17.7% (44/248)</td>
</tr>
<tr>
<td><strong>Distal Target Vessel</strong></td>
<td></td>
</tr>
<tr>
<td>P2/P3</td>
<td>5.2% (13/248)</td>
</tr>
<tr>
<td>TP Trunk</td>
<td>10.1% (25/248)</td>
</tr>
<tr>
<td>Anterior tibial</td>
<td>41.5% (103/248)</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>22.2% (55/248)</td>
</tr>
<tr>
<td>Peroneal</td>
<td>21.4% (53/248)</td>
</tr>
</tbody>
</table>

*Protocol specified balloon-to-vessel ratio of 1:1 (visual estimate)
†Site-reported baseline lesion length: 116 ± 100 (277)
Distal Delivery With No Fracture
(ITT population; core lab adjudicated)

<table>
<thead>
<tr>
<th>Index Procedure Details</th>
<th>Mean ± SD or % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dissections per patient</td>
<td>1.4 ± 0.6 (229)</td>
</tr>
<tr>
<td>Dissection length (mm)</td>
<td>24 ± 18 (341)</td>
</tr>
<tr>
<td>Post-PTA NHLBI Dissection Grade (Pre-Tack)</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>21.4% (49/229)</td>
</tr>
<tr>
<td>B</td>
<td>39.3% (90/229)</td>
</tr>
<tr>
<td>C</td>
<td>11.8% (27/229)</td>
</tr>
<tr>
<td>D</td>
<td>26.6% (61/229)</td>
</tr>
<tr>
<td>E</td>
<td>0.9% (2/229)</td>
</tr>
<tr>
<td>Device success</td>
<td><strong>96.5% (303/314)</strong></td>
</tr>
<tr>
<td>Bail out stent</td>
<td>1.3% (3/233)</td>
</tr>
<tr>
<td><strong>To Tacked segment</strong></td>
<td><strong>0.4% (1/233)</strong></td>
</tr>
<tr>
<td>Total # of Tacks deployed</td>
<td>918</td>
</tr>
<tr>
<td>Tacks per patient</td>
<td>4.0 ± 2.8 (230)</td>
</tr>
</tbody>
</table>

100% dissection resolution per core lab

35% of Tack implants were deployed in the mid and distal tibials

<table>
<thead>
<tr>
<th>12 Month X-ray of Tack Implant(s)</th>
<th>% (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fracture</td>
<td>0% (0/146)</td>
</tr>
<tr>
<td>Migration</td>
<td>0% (0/146)</td>
</tr>
<tr>
<td>Embolization</td>
<td>0% (0/146)</td>
</tr>
</tbody>
</table>
Met All Primary and Secondary Endpoints

(ITT population; core lab adjudicated)

- **Primary Safety:** MALE + POD at 30d
  - 1.3% (3/228)
  - 95% CI [0.3%, 3.8%]

- **Primary Efficacy:** Freedom from 6m MALE + 30d POD
  - OPG: 12%
  - 95% CI [91.9%, 97.8%]

- **Secondary Efficacy:** 6m Tacked Segment Patency
  - OPG: 64%
  - 95% CI [77.0%, 86.0%]

- **Unpowered Secondary:** 6m Target Limb Salvage
  - OPG: 20%
  - 95% CI [95.8%, 99.7%]
Tacked segment patency: 12m DUS flow/no flow in Tacked segment (Tack implant + 5mm artery proximal and distal; Tacks within 1cm are considered same segment)

Target lesion patency: 12m DUS flow/no flow in PTA treated length (154 ± 110mm)

81.3% @ 360d (Tacked segment)

78.6% @ 360d (target lesion)
Freedom from Loss of Patency and CD-TLR*

(Target lesion patency (post hoc): DUS flow/no flow in entire PTA treated length (154 ± 110mm) and freedom from CD-TLR

*Post hoc analysis; has not been reviewed by US FDA
Freedom from CD-TLR

(ITT population; CEC adjudicated)

- 92.3% @ 180d
- 83.1% @ 360d

<table>
<thead>
<tr>
<th>Event</th>
<th>0</th>
<th>30</th>
<th>180</th>
<th>210</th>
<th>360</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Risk</td>
<td>232</td>
<td>225</td>
<td>182</td>
<td>167</td>
<td>100</td>
</tr>
<tr>
<td>All ITT</td>
<td>100%</td>
<td>100%</td>
<td>92.3%</td>
<td>89.7%</td>
<td>83.1%</td>
</tr>
</tbody>
</table>
**Target Limb Salvage**

(ITT population; by baseline RC*)

- **98.6% @ 180d (All)**
- **98.4% @ 180d (RC 4/5)**
- **96.8% @ 360d (All)**
- **96.1% @ 360d (RC 4/5)**

*Post hoc analysis; has not been reviewed by US FDA*
Amputation-Free Survival

(ITT population; by baseline RC*)

- 95.9% @ 180d (All)
- 95.1% @ 180d (RC 4/5)*
- 89.3% @ 360d (All)
- 89.0% @ 360d (RC 4/5)*

*Post hoc analysis; has not been reviewed by US FDA
Improvement in TBI and Baseline Wounds
(ITT population; site-reported)

**Toe Brachial Index**

![Graph showing changes in Toe Brachial Index from Baseline to 6m and 12m with statistical significance noted as p<0.0001*.](image)

**Index Wound Status at 12m**

<table>
<thead>
<tr>
<th>Status</th>
<th>% (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound(s) Healed</td>
<td>68.6% (85/124)</td>
</tr>
<tr>
<td>with minor amputation†</td>
<td>11.3% (14/124)</td>
</tr>
<tr>
<td>with major amputation†</td>
<td>2.4% (3/124)</td>
</tr>
<tr>
<td>Wound(s) Improving</td>
<td>4.0% (5/124)</td>
</tr>
<tr>
<td>with minor amputation†</td>
<td>0.8% (1/124)</td>
</tr>
<tr>
<td>Wound(s) Unchanged</td>
<td>4.8% (6/124)</td>
</tr>
<tr>
<td>Wound(s) Worsening</td>
<td>2.4% (3/124)</td>
</tr>
<tr>
<td>Wound(s) amputated prior to 12m; missing 12m data†</td>
<td>5.7% (7/124)</td>
</tr>
</tbody>
</table>

*Reported by wound
†Post-hoc analysis; has not been reviewed by FDA

*Wilcoxon Signed Rank test
Sustained Improvement in Rutherford (ITT population)

60.4% of patients improved ≥3 classes

79.1% of patients improved to ≤RC2
Sustained Quality of Life Improvement  
(patient reported; ITT population)

**MOBILITY**
- % with NO LIMITATIONS (n=180)
- $p<0.0001^*$

**PAIN**
- $p<0.0001^*$

**DAILY ACTIVITY**
- $p<0.0001^*$

**GENERAL HEALTH**
- $p=0.0004^†$

*Generalized McNemar’s test

†Wilcoxon Signed Rank test
Tack: A New Therapy for BTK Dissection Repair

**First BTK vascular implant to achieve FDA approval**
- Unique trial: first BTK IDE study to enroll **100% dissected vessels**
- Tack implant repaired **100%** of post-PTA dissections

12-month results:
- **No** fracture, migration or embolization
- **81.3%** K-M Tacked segment patency
- **83.1%** K-M freedom from CD-TLR
- **Sustained improvement** in Rutherford, TBI and QoL

CLTI (Rutherford 4 & 5) patient outcomes:*  
- **96.1%** K-M target limb salvage
- **89.0%** amputation-free survival

*Post hoc analysis; has not been reviewed by US FDA