From Chocolate to Hawk: Vessel Preparation for Improved Outcomes

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant/Research Support</td>
<td>None</td>
</tr>
<tr>
<td>Consulting Fees/Honoraria</td>
<td>Abbott, Endologix, Boston Scientific, CSI, Medtronic, Bard</td>
</tr>
<tr>
<td>Major Stock Shareholder/Equity</td>
<td>None</td>
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<tr>
<td>Royalty Income</td>
<td>None</td>
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<tr>
<td>Ownership/Founder</td>
<td>None</td>
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<td>Intellectual Property Rights</td>
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<td>Other</td>
<td>None</td>
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<td></td>
<td>VIVA Board Member</td>
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</table>
What do We Mean by “Vessel Prep”? 

• We want to “pre-treat” the lesion safely such that we leave definitive therapy options wide open AND increase their effectiveness

• BTK our Vessel prep may be “stand alone therapy”

• For femero-popliteal lesions we want to maximize drug delivery to the vessel wall, while minimizing dissection and maximizing lumen (IF DCB is strategy, help it work best)
What Does “Vessel Prep” before DCB Mean? - 2

• In my opinion, it does **NOT necessarily** mean atherectomy

• Vessel Prep **Goals**:
  – Pretreat such that ≥ 1:1 DCB doesn’t dissect
  – Remove impediments to drug delivery
  – Avoid drug loss on way to lesion
  – Maximize DCB expansion & vessel contact
  – Minimize dissections & issues w/ Prep, Rx

*One goal: Maximize luminal gain while minimizing dissection*
My “Vessel Prep” Algorithm

- Does the lesion look like it “needs” or would benefit from atherectomy before DCB?
  - *If yes, individualized atherectomy w/ dEPD*

- If not, perform PTA or specialty PTA with balloon 1mm ≤ DCB, on roadmap
  - *LONG, slow inflations; no “geographic miss”*

- ≥1.1:1 DCB with good technique

- Accept less than perfect results; only stent prn
  - *If stenting, still need vessel prep (interwoven or nitinol)*
Limitations of Endovascular Therapy

4 Key factors continue to pose a challenge to the use of endovascular approaches as primary therapy

1. Flow Limiting Dissection
2. Lesion Length
3. Calcium
4. Provisional Stenting
## Limitations of Endovascular Treatment

### Flow Limiting Dissection

<table>
<thead>
<tr>
<th>Product</th>
<th>Study</th>
<th>Dissection rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lutonix™</strong> 035</td>
<td>LEVANT 2&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Grade C</td>
</tr>
<tr>
<td></td>
<td>LUTONIX Long Lesion&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Grade C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.5% (8/316)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.2% (10/82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.2% (1/82)</td>
</tr>
<tr>
<td><strong>Stellarex™</strong></td>
<td>ILLUMENATE EU&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Flow-limiting</td>
</tr>
<tr>
<td></td>
<td>ILLUMENATE Global&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Grade D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>19.7% (81/416)</td>
</tr>
<tr>
<td></td>
<td>ILLUMENATE Pivotal&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Grade E/F</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2% (1/416)</td>
</tr>
<tr>
<td><strong>IN.PACT™ Admiral™ DCB</strong></td>
<td>IN.PACT SFA&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Grades D – F</td>
</tr>
<tr>
<td></td>
<td>IN.PACT Global ISR&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Grades D – F</td>
</tr>
<tr>
<td></td>
<td>IN.PACT Global CTO&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Grades D – F</td>
</tr>
<tr>
<td></td>
<td>IN.PACT Global Long Lesion&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Grades D – F</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0% (0/221)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.7% (7/149)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23.6% (30/127)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.9% (24/161)</td>
</tr>
</tbody>
</table>

2. Bard Lutonix Instructions for Use. BAW1387400r3.
Limitations of Endovascular Treatment

Lesion Length

Increased lesion length is an independent predictor of decreased patency.

Primary patency rates may be calculated differently, and therefore may not be directly comparable. Chart is for illustration purposes only.

- Ansel, G. VIBRANT 1 year results. LINC 2010.
- Innova IFU.
- Jaff, M. STROLL 3 year results. ISET 2014.
Limitations of Endovascular Treatment

Calcium

- Calcium is a potential barrier to optimal drug absorption
- Calcium distribution and severity may affect late lumen loss (LLL) and primary patency

Primary patency defined as freedom from restenosis by duplex based on PSVR<2.4 and TLR
Limitations of Endovascular Treatment

Provisional Stenting

- DCB use in real-world registries enrolling more complex disease is associated with increased provisional stenting.
- Provisional stent rates of 40-47%

Primary patency rates may be calculated differently, and therefore may not be directly comparable. Chart is for illustration purposes only.

2 Strategies to Maximize Vessel Prep

- Both strategies have the potential to maximize luminal gain AND decrease dissections*
- *Both strategies have data to support this
- Both strategies *may* increase the effectiveness of DCB’s and improve drug delivery, and have potential as an effective “stand-alone” BTK Rx
- These strategies are specialty balloons (e.g. Chocolate balloon) and (Directional) Atherectomy (e.g. Hawks)
Vessel Preparation
Chocolate™ PTA Balloon Catheter

**Braided Catheter Shaft:**
Provides robust pushability to reach and cross lesions.

**Nitinol Constraining Structure:**
Creates **PILLOWS** and **GROOVES** in balloon that provide predictable, uniform and atraumatic dilation.

**Nylon, Semi Compliant Balloon:**
Allows for optimal balloon pillow formation

**Distal and Proximal Marker Bands:**
Provides visibility and accuracy of placement under fluoroscopy

**Tapered Tip:**
Enables lower entry profile for optimal lesion access
Unique nitinol constraining structure reduces the strain and trauma induced on the vessel wall during inflation through the use of "pillows" and "grooves" to relieve stress, modify the plaque and uniformly distribute circumferential forces to minimize vessel wall trauma.
CHALLENGES WITH STANDARD PTA

- Uncontrolled PTA Balloon Inflation

  Can lead to

  Stress & deformation to vessel wall = Vessel Trauma

Types of Stresses

1. Torsional (Twisting)
2. Radial (Expanding)
3. Longitudinal (Elongating)

Flow limiting vessel dissection
PTA verses Chocolate PTA inflation

Conventional Balloon

Chocolate® PTCA

0.0 ATM
Vessel Preparation
Chocolate™ PTA Balloon Catheter

Conventional PTA Balloon
Nominal > Nominal

Chocolate™ Balloon
Nominal > Nominal

Grooves allow for plaque extrusion / remodeling
Higher pressure enhances pillows
**Chocolate Bar Study: Overview**

**LARGE, PROSPECTIVE, POST MARKET STUDY**

<table>
<thead>
<tr>
<th>Study Dates: June 2012-December 2014</th>
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</thead>
<tbody>
<tr>
<td>Principal Investigator</td>
</tr>
<tr>
<td>Number of Sites</td>
</tr>
<tr>
<td>Patients Enrolled</td>
</tr>
<tr>
<td>BTK</td>
</tr>
<tr>
<td>With planned follow-up through 6 months</td>
</tr>
<tr>
<td>ATK</td>
</tr>
<tr>
<td>With planned follow-up through 12 months</td>
</tr>
</tbody>
</table>

**Inclusion Criteria**

- Any ATK or BTK lesion with at least 1 vessel runoff successfully crossed with a guidewire
- Use of atherectomy/re-entry devices accepted

**Exclusion Criteria**

- Presence of a flow-limiting dissection at the target lesion prior to use of the Chocolate™* PTA balloon (secondary to the use of another device)
- Patients with Rutherford 6
- Chocolate™* PTA balloon not used in accordance with study protocol (2 min inflation to at least nominal pressure)
## Chocolate Bar Study
### PATIENT & LESION CHARACTERISTICS

<table>
<thead>
<tr>
<th>Population</th>
<th>ATK** N = 262</th>
<th>BTK N = 226</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average Age (yrs)</strong></td>
<td>69.7</td>
<td>71.5</td>
</tr>
<tr>
<td>Male</td>
<td>61.1% (160)</td>
<td>65.9% (149)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>50.4% (132)</td>
<td>58.8% (133)</td>
</tr>
<tr>
<td>CLI</td>
<td>32.1% (84)</td>
<td>55.8% (126)</td>
</tr>
<tr>
<td>Rutherford 5+</td>
<td>19.1% (50)</td>
<td>37.6% (85)</td>
</tr>
<tr>
<td>Total Occlusion</td>
<td>23.0% (60/261)</td>
<td>41.1% (99/241)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calcification</th>
<th>ATK** N = 261</th>
<th>BTK N = 229</th>
</tr>
</thead>
<tbody>
<tr>
<td>None / Mild</td>
<td>36.5% (93/255)</td>
<td>67.7% (155/229)</td>
</tr>
<tr>
<td>Moderate</td>
<td>43.5% (111/255)</td>
<td>30.1% (69/229)</td>
</tr>
<tr>
<td>Severe</td>
<td>2.2% (5/229)</td>
<td>20.0% (51/255)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Lesion Length</th>
<th>ATK** N = 262</th>
<th>BTK N = 226</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>83.5 mm</td>
<td>66.0 mm</td>
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</table>
# Chocolate Bar Study

## OUTCOMES

<table>
<thead>
<tr>
<th>Procedural Success</th>
<th>ATK** (n = 262)</th>
<th>BTK (n = 226)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedom from Flow Limiting Dissections* (Site Reported)</td>
<td>97.7%</td>
<td>99%</td>
</tr>
<tr>
<td>Freedom from Flow Limiting Dissections* (Adjudicated)</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Achieved &lt;30% Diameter Stenosis (Adjudicated)</td>
<td>85.1%</td>
<td>84.6%</td>
</tr>
<tr>
<td>Freedom from Bail-Out Stenting</td>
<td>98.4%</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Outcomes (Kaplan Meier)</th>
<th>ATK** (n = 262)</th>
<th>BTK (n = 226)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedom from Target Lesion Revascularization</td>
<td>78.5%</td>
<td>88.9%</td>
</tr>
<tr>
<td>Freedom from Major Unplanned Amputation</td>
<td>97.2%</td>
<td>96.7%</td>
</tr>
<tr>
<td>Freedom from All-Cause Mortality</td>
<td>93.3%</td>
<td>97.1%</td>
</tr>
</tbody>
</table>

*Flow Limiting Dissections defined as: Type E - Persistent luminal filling defect with delayed run-off of the contrast material in the distal lumen and Type F - Filling defect accompanied by total occlusion

** many ATK patients had concurrent BTK disease
Dissection Rate in Context
Comparison Across Standard and Specialty PTA

**ATK**
- ABSOLUTE PTA Arm: 16%
- RESILIENT PTA Arm: 40%
- Chocolate BAR: 0%

**BTK**
- Bosiers PTA Arm: 12% 12%
- Odink PTA Arm: 8%
- Chocolate BAR: 0% 1%

% Flow-limiting dissections
% Bail-out stents placed

3) Data on file with Medtronic – CLR782: Final Study Report The Chocolate BAR by TriReme Medical, LLC
Vessel Preparation
Directional Atherectomy

SilverHawk™, TurboHawk™, HawkOne™ plaque excision systems

DEFINITIVE LE
DEFINITIVE AR
DEFINITIVE LE
Study Overview

Prospective Multinational, Single Arm Study
Core-Lab Adjudicated*

Objective: Evaluate the effectiveness of standalone SilverHawk™/TurboHawk™ plaque excision systems for endovascular treatment of peripheral arterial disease in the femoropopliteal and tibioperoneal arteries.

Primary Outcomes

Claudicant: Primary Patency by Duplex Ultrasound at 12 months (PSVR ≤2.4 with no clinically-driven reintervention)

CLI: Freedom From Major Unplanned Amputation at 12 months

800 Patients

47 Sites
US and Europe

Follow up: 1 year

*VasCore DUS Core Laboratory, Boston, MA and SynvaCor Angiographic Core Laboratory, Springfield, IL.

DEFINITIVE LE
Results

Primary Patency At 12 Months (Kaplan-meier)

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Claudicant n = 598</th>
<th>CLI n = 201</th>
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<tbody>
<tr>
<td>Primary Patency</td>
<td>75%</td>
<td>77%</td>
</tr>
<tr>
<td></td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>Mean Length (cm)</td>
<td>7.5 ± 5.3</td>
<td>7.2 ± 5.5</td>
</tr>
<tr>
<td></td>
<td>0.381</td>
<td></td>
</tr>
<tr>
<td>Flow-Limiting Dissection Rate</td>
<td>2.2% (13)</td>
<td>2.5% (5)</td>
</tr>
<tr>
<td></td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Bailout Stenting</td>
<td>--</td>
<td>3.2%</td>
</tr>
<tr>
<td>Primary Patency defined as: duplex ultrasonography measurement of the peak systolic velocity ratio (PSVR) ≤ 2.4 at the target lesion(s) with no clinically-driven reintervention within the target segment.</td>
<td></td>
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</tr>
</tbody>
</table>
Pilot Study to assess the effect of treating a lesion with directional atherectomy followed by drug-coated balloon vs. drug-coated balloon alone.

Primary Outcome:
Target Lesion Percent Lesion Stenosis at 1 year (Angiographic Core Lab)

121 Patients
10 Centers in Europe
Follow up: 1 year
Atherectomy and DCB Efficacy: Clinical Evidence

- **DEFINITIVE AR**: directional atherectomy + DCB vs DCB alone
- Adjunctive atherectomy may improve procedural and clinical outcomes following DCB treatment of the SFA and/or popliteal artery, particularly for longer or severely calcified lesions

### Procedural Results

<table>
<thead>
<tr>
<th></th>
<th>DCB</th>
<th>Ath + DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Technical Success</strong>*</td>
<td>64.2%</td>
<td>89.6%</td>
</tr>
<tr>
<td><strong>Bail-out Stent</strong></td>
<td>3.7%</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Flow-limiting Dissection</strong></td>
<td>19%</td>
<td>2%</td>
</tr>
</tbody>
</table>

### Duplex Ultrasound Patency at 12-months

- **Lesions >10 cm**
  - DCB: 86% (n=31)
  - Ath + DCB: 97% (n=23)
- **Severely Calcified**
  - DCB: 63% (n=8)
  - Ath + DCB: 70% (n=27)
- **All patients**
  - DCB: 90% (n=54)
  - Ath + DCB: 93% (n=48)

---

Zeller, VIVA 2014.

*Technical success: Defined as ≤ 30% residual stenosis following the protocol-defined treatment at the target lesion as determined by the Angiographic Core Laboratory. DCB, drug-coated balloon; DUS, duplex ultrasound; SFA, superficial femoral artery.
12-Month Patency: DA-ART RCT Patients

Minimizing residual stenosis with directional atherectomy may be important

DAART resulted in a significantly larger minimum lumen diameter (MLD) following the protocol-defined treatment in DEFINITIVE AR

Zeller, VIVA 2015

Slide borrowed w/ permission from K. Rocha-Singh, MD
DEF AR Study-2-Yr Extension

Freedom from TLR: ≤30% residual stenosis

83.3

55.2

Δ +28.1%

≤30% Residual Stenosis Post-DA
>30% Residual Stenosis Post-DA

Freedom from TLR

Slide borrowed w/ permission from K. Rocha-Singh, MD
Directional Atherectomy + Drug Coated Balloon To Treat Long Calcified Femoropopliteal Artery Lesions
Live case right after left leg PVI

Severe CA++
LIVE Case right more severe disease
Larger atherectomy popliteal with dEPD

Angio improving
Angio after Chocolate 😊

*(remember initial CA++; CTO)*
Prolonged DCB’s
Angio and IVUS after DCB
Final popliteal/ trifurcation and runoff angios
Conclusions

• Optimal “vessel preparation” should maximize luminal gain while minimizing dissection
• Both Chocolate Specialty PTA and Directional Atherectomy have large trial data showing ↑ luminal gain with ↓ dissection rates compared to historical data of other technologies
• These features suggest potential benefit for these vessel preparation strategies before DCB
• The VIVA REALITY Trial is prospectively studying DA + DCB in long CA++ lesions
Thank You Very Much for Your Attention!
From Chocolate to Hawk: Vessel Preparation for Improved Outcomes

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