Next Steps in Drug Eluting Stent for BTK Intervention

Jihad A. Mustapha, MD, FACC, FSCAI
Advanced Cardiac & Vascular Amputation Prevention Centers
Grand Rapids, MI USA
• IMPORTANT INFORMATION: These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician’s professional judgment in light of all available information for the case at hand.

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• Results from case studies are not necessarily predictive of results in other cases. Results in other cases may vary.
Disclosure

Speaker name: Jihad A. Mustapha

I have the following potential conflicts of interest to report:

- [X] Consulting: Abbott Vascular, Bard Peripheral Vascular, Boston Scientific, Cagent Vascular, Cardiovascular Systems, Inc., Cook Medical, Medtronic, PQ Bypass, Spectranetics, Terumo Medical
Eluvia™ Drug-Eluting Vascular Stent System

• CE Mark February 2016
• Innova stent platform
  • Self-expanding nitinol
• Biostable polymer matrix
• Paclitaxel

• 6F Tri-axial SDS, 0.035” guidewire compatible
• Blue Tri-Ax shaft fixed as the clear middle shaft is retracted releasing stent during deployment
Eluvia Coating Design

• Dual Layer System
• Conformal Coating for Both Layers
• Primer Layer (PBMA): Promotes Adhesion of Active Layer to Stent
• Active Layer (PTx, PVDF-HFP)—Controls Release of Paclitaxel
  • 0.167µg PTx/mm² stent surface area

PBMA Primer Layer

Stent

Paclitaxel/PVDF-HFP Active Layer

Boston Scientific Data on File.
BSC Peripheral BMS/DES Clinical Program

SuperNOVA (BMS)
Prospective, multicentre, single-arm, open label
N = 299 (3 year follow-up complete)

MAJESTIC (DES)
Prospective, multicentre, single-arm, open label
N = 57 (3 year follow-up complete)

IMPERIAL (DES)
Prospective, multicentre, RCT 2:1 (Eluvia : ZilverPTX)
N = 524 (including RCT, PK, LL. Enrollment Complete)

EMINENT (DES/BMS)
Prospective, multicentre, RCT 2:1 (Eluvia : BMS)
N = 750 (Enrolling)

REGAL (DES)
Prospective, multicentre, single-arm, open label
N = 500 (Enrolling)

DES BTK (DES)
Prospective, multicentre, RCT 2:1 (DES BTK : PTA) & single-arm
N = 201 & N = 100

Caution: Eluvia is an investigational device limited under US law for investigational use only. Not available for sale in the U.S.
Subgroup Analysis – 3 Years
Severe Calcification, Occlusion, Diabetes

3-Year Freedom from TLR

- Low reintervention rates among patients with challenging medical and lesion characteristics at baseline

<table>
<thead>
<tr>
<th></th>
<th>Occlusion (N=26)</th>
<th>Severe Calcification (N=37)</th>
<th>Diabetes (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>fTLR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>84.3%</td>
<td>85.5%</td>
<td>82.4%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Kaplan-Meier estimate at 1095 days.

Impact of Fluoropolymer-Based Paclitaxel Delivery on Neointimal Proliferation and Vascular Healing
A Comparative Peripheral Drug-Eluting Stent Study in the Familial Hypercholesterolemic Swine Model of Femoral Restenosis

Pawel Gasior, MD, PhD; Yanping Cheng, MD; Andres F. Valencia, MD; Jenn McGregor, BS; Gerard B. Conditt, RCIS; Grzegorz L. Kaluza, MD, PhD; Juan F. Granada, MD

• Familial hypercholesterolemic swine model of femoral restenosis
• Fluoropolymer-coated paclitaxel eluting stent (Eluvia) vs polymer-free paclitaxel-coated stent vs bare metal stent
• 30 days- Quantitative vascular angiography and optical coherence tomography
• 90 days- Histological evaluation

## FP-PES:PES:BMS Preclinical Study

### OCT and Corresponding Histology at 90 days

<table>
<thead>
<tr>
<th></th>
<th>FP-PES</th>
<th>PES</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histology</strong></td>
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</tr>
<tr>
<td><strong>OCT</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Proximal</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Medial</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Distal</strong></td>
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</table>

**Eluvia DES**

**Zilver DES**

BMS, bare metal stent; FP-PES, fluoropolymer-paclitaxel eluting stent; OCT, optical coherence tomography; PES, paclitaxel eluting stent

Preclinical results may not necessarily be indicative of clinical performance.
FP-PES:PES:BMS Preclinical Study

OCT at 30 and 90 days

OCT results at 30- and 90-day follow-up demonstrated greater lumen diameter and smaller neointimal proliferation expressed by neointimal thickness, neointimal area, and % area stenosis in fluoropolymer-based paclitaxel-eluting stent (FP-PES) when compared with PES and BMS.
Scientific Poster
Comparative biomechanics and vascular healing response of 3 contemporary stents in balloon-predilated femoral arteries of familial hypercholesterolemic swine

Miguel Montero-Baker

Wednesday, January 31st: 9:00 - 10:40
Original research: PVD, SFA, femoral
The Case for DES below-the-knee

<table>
<thead>
<tr>
<th>Disease State Implications</th>
<th>Clinical Data</th>
<th>Cost</th>
</tr>
</thead>
</table>
| • Calcification not an impediment for drug delivery via DES  
• CTOs, long lesions, and vessel recoil favor scaffold | At least four RCTs have shown efficacy of coronary DES in BTK vessels  
Two RCTs with DCB below-the-knee have not shown efficacy | Cost considerations likely to favor PTA + BTK scaffold (versus PTA + ATHX + DCB + potential bailout) |
Ankle joint

Proximal tibials

Non balloon expandable DES zone

Balloon expandable DES zone

Distal tibials

BTK/BTA Scaffold

Pedal arteries

Ankle joint

Non balloon expandable DES zone

Non balloon expandable DES zone
SAVAL™ DES BTK stent

- Nitinol Self-Expanding Stent
  - Flexible crush resistant scaffold
  - Diameter compliant
- PTx drug coating (PBMA/PVDF)

Differentiated technology has been selected for Expedited Access Pathway (EAP) designation by FDA

*CAUTION: Investigational device and not available for sale in the U.S.
### BSC Peripheral BMS/DES Clinical Program

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Enrollment Status</th>
<th>N</th>
<th>Follow-up</th>
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<tbody>
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<td><strong>SuperNOVA</strong> (BMS)</td>
<td>Prospective, multicentre, single-arm, open label</td>
<td></td>
<td><strong>299</strong></td>
<td>3 year complete</td>
</tr>
<tr>
<td><strong>MAJESTIC</strong> (DES)</td>
<td>Prospective, multicentre, single-arm, open label</td>
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<td><strong>57</strong></td>
<td>3 year complete</td>
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<tr>
<td><strong>IMPERIAL</strong> (DES)</td>
<td>Prospective, multicentre, RCT 2:1 (Eluvia : ZilverPTX)</td>
<td></td>
<td><strong>524</strong></td>
<td>Enrollment Complete</td>
</tr>
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<td><strong>EMINENT</strong> (DES/BMS)</td>
<td>Prospective, multicentre, RCT 2:1 (Eluvia : BMS)</td>
<td></td>
<td><strong>750</strong></td>
<td>Enrolling</td>
</tr>
<tr>
<td><strong>REGAL</strong> (DES)</td>
<td>Prospective, multicentre, single-arm, open label</td>
<td></td>
<td><strong>500</strong></td>
<td>Enrolling</td>
</tr>
<tr>
<td><strong>SAVAL</strong> (DES)</td>
<td>Prospective, multicentre, RCT 2:1 (DES BTK : PTA) &amp; single-arm</td>
<td></td>
<td><strong>201 &amp; 100</strong></td>
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</tbody>
</table>

**Legend:**
- **SFA**: Superficial femoral artery
- **BTK**: Below-the-knee
- **BMS**: Bare metal stent
- **DES**: Drug-eluting stent
- **LL**: Long lesions
- **PK**: Pharmacokinetics
- **PTA**: Percutaneous transluminal angioplasty
- **RCT**: Randomized controlled trial

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The SAVAL™ Pivotal Trial

A Randomized Trial comparing the Drug-Eluting Stent (DES) Below the Knee (BTK) Vascular Stent System vs Percutaneous Transluminal Angioplasty (PTA) Treating Infrapopliteal Lesions in Subjects With Critical Limb Ischemia

- Planned Global Pivotal Trial
- Randomized DES vs PTA
- 6 Month Primary Patency Endpoint
- FDA EAP+ Breakthrough Pathway
- First Ever EAP in Peripheral Branch of FDA
- Anticipated Enrollment Start 2018

*CAUTION: Investigational device and not available for sale in the U.S.
*FDA’s Expedited Access Pathway (EAP) program is intended for breakthrough medical devices that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases.
Why pursue DES below the knee?

• Presence of long lesions, occlusions, and calcification less detrimental for stent-based drug delivery

• Signals from SFA and preclinical studies suggest Eluvia performance aligns with desired characteristics for BTK treatment

• SAVAL study to investigate DES BTK performance vs PTA
Next Steps in Drug Eluting Stent for BTK Intervention

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