Boston Scientific’s ELUVIA Drug-Eluting Stent and Coronary Paclitaxel-Eluting Stent Clinical Experience

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Boston Scientific
I. Introduction

II. Overview of the ELUVIA™ Drug-Eluting Stent (DES)

III. Coronary data supports safety of paclitaxel and ELUVIA DES

IV. 5-year data for paclitaxel-eluting stents in coronary and peripheral vasculature show no mortality signal

V. ELUVIA DES shows no mortality signal

VI. ELUVIA DES has demonstrated a positive benefit-risk profile

VII. Conclusion
• Paclitaxel identified as effective antirestenotic agent
• Polymer matrix enables controlled, sustained drug elution
• Paclitaxel localized in the stented region
  – No measurable systemic drug at 30 min post-implant
• Low dose
  – 0.167 µg/mm² dose density

Design Principles of the ELUVIA DES

Stent

Paclitaxel/Polymer Active Layer

Primer Layer

Diffusion-controlled low-dose elution over time
ELUVIA DES is Differentiated from Other Paclitaxel-Coated Technologies

<table>
<thead>
<tr>
<th></th>
<th>Paclitaxel-Eluting</th>
<th>Zilver PTX Stent</th>
<th>DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ELUVIA DES</td>
<td>Zilver PTX Stent</td>
<td>IN.PACT</td>
</tr>
<tr>
<td>Biostable Polymer</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Excipient</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Amorphous Coating Morphology</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Paclitaxel Dose Density (µg/mm²)</td>
<td>0.167</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td>Total Dose (6 mm x 120 mm)</td>
<td>409 µg</td>
<td>1103 µg</td>
<td>8448 µg</td>
</tr>
<tr>
<td>Diffusion-Controlled Elution</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Particulate Counts (≥10µm size)</td>
<td>1381</td>
<td>11,928</td>
<td>567,432</td>
</tr>
</tbody>
</table>

Only device with a polymer to elute drug over time
Low dose density and low total dose are effective

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*Simulated use in a tortuous vessel model under clinically relevant flow conditions. Device sizes for particulates testing: 6mmx120mm stents, 6mmx80mm balloons. BSC Data on file.
Data from ELUVIA, Zilver PTX, Lutonix, Stellarex and IN.PACT DFUs. Abbreviations: DCB, drug-coated balloon; DES, drug-eluting stent.
ELUVIA DES and coronary DES design principles are identical

<table>
<thead>
<tr>
<th>Vasculature</th>
<th>Peripheral</th>
<th>Coronary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biostable Polymer</td>
<td>✓ (PVDF-HFP)</td>
<td>✓ (SIBS)</td>
</tr>
<tr>
<td>Amorphous Coating Morphology</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Low Dose</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Total Dose on Stent</td>
<td>135 µg</td>
<td>282 µg</td>
</tr>
<tr>
<td>Diffusion-Controlled Elution</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

ELUVIA DES is Comparable to Coronary DES

Abbreviations: DES, drug-eluting stent; PVDF-HFP, poly(vinylidene fluoride-co-hexafluoropropylene); SIBS, poly(styrene-block-isobutylene-block-styrene). Stent sizes for total dose: ELUVIA DES 6.0 mm x 40 mm, Coronary 4.0 mm x 38 mm.
• Atherosclerosis is a systemic disease affecting coronary and peripheral arteries
• Response to injury (restenosis) phases are the same in peripheral and coronary vascular beds
• Paclitaxel anti-restenotic mechanism of action on vessels is the same

Coronary paclitaxel-eluting stent data inform the safety profiles of paclitaxel and ELUVIA DES
Paclitaxel-Eluting Coronary Stent Design and Clinical Use are Applicable to ELUVIA DES

• >15,000 patients with CAD have been studied in clinical trials of coronary paclitaxel-eluting stents
• >4000 in double blinded RCTs
  – Independent CECs, DSMBs
  – Designed to be pooled
  – Common event definitions
  – High compliance with follow-up at 5 years

Totality of TAXUS trial data support paclitaxel and ELUVIA DES safety

Abbreviations: CAD, coronary artery disease; CEC, Clinical Events Committee; DES, drug-eluting stent; DSMB, Data Safety Monitoring Board; RCT, randomized controlled trial.
No all-cause mortality signal in meta-analysis of paclitaxel-eluting stent vs BMS

Cumulative event rate data on file. Abbreviations: BMS, bare metal stent; CAD, coronary artery disease; PTx, paclitaxel.
5-Year Follow-up of Paclitaxel-Eluting Stent for High-Risk PAD (Critical Limb Ischemia)

- RCT of infrapopliteal stent placement to treat high-risk PAD/CLI
- Similar survival rates for paclitaxel-eluting vs bare control through 5 years
- Paclitaxel-eluting stent treatment reduced major amputation rate by 57% at 5 years (19.3% vs 34.0%)

No difference in all-cause mortality between paclitaxel-eluting stent and BMS in high-risk PAD

In Summary

• Paclitaxel is safe and effective
• Design principles of ELUVIA DES and coronary paclitaxel-eluting stents are identical
• No all-cause mortality signal in TAXUS studies of paclitaxel-eluting stents
• Any systemic effect of paclitaxel would have been observed in the TAXUS studies
Mortality, Benefit-Risk, and Ongoing Studies of ELUVIA DES

Robert A. Lookstein, MD FSIR FAHA
Professor of Radiology and Surgery
Vice Chair and Chief
Division of Interventional Radiology
Mount Sinai Medical Center
### BSC Sponsored Studies of ELUVIA DES: Three Independently Adjudicated Trials

<table>
<thead>
<tr>
<th>Clinical Study</th>
<th>Design</th>
<th>Total Enrollment</th>
<th>Number of ELUVIA DES Patients</th>
<th>Protocol Follow-up</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAJESTIC</td>
<td>Single arm ELUVIA DES</td>
<td>57</td>
<td>57</td>
<td>3 years</td>
<td>Complete</td>
</tr>
<tr>
<td>IMPERIAL</td>
<td>RCT (2:1) ELUVIA DES vs Zilver PTX</td>
<td>524</td>
<td>372</td>
<td>5 years</td>
<td>2 year follow-up complete</td>
</tr>
<tr>
<td>EMINENT</td>
<td>RCT (2:1) ELUVIA DES vs BMS</td>
<td>750</td>
<td>500</td>
<td>3 years</td>
<td>Enrolling</td>
</tr>
</tbody>
</table>

**Significant ongoing large randomized controlled trials with ELUVIA DES**

**MAJESTIC enrollment values include RCT, Long Lesions and Pharmacokinetics Sub-studies.**

*Abbreviations: BMS, bare metal stent; DES, drug-eluting stent; RCT, randomized controlled trial.*
Mortality rate for ELUVIA comparable to FDA PTA Reference

No mortality signal for ELUVIA DES

MAJESTIC follow-up is final at 3 years. IMPERIAL follow-up is complete through 2 years and ongoing through 5 years. As-treated ELUVIA patients. FDA PTA reference based on FDA Executive Summary. Abbreviations: DES, drug-eluting stent; PTA, percutaneous transluminal angioplasty.
Predictors of Mortality Typical for PAD Patients: Diabetes and Age

Predictor Analysis of 2 Year Mortality in MAJESTIC and IMPERIAL (N=540 ELUVIA DES & Zilver PTX)

**Multivariable Model with Dose Variable**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel Dose (100µg)</td>
<td>0.04</td>
<td>0.04</td>
<td>1.04 (0.96, 1.00)</td>
<td>0.3543</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.12</td>
<td>0.36</td>
<td>3.07 (1.52, 6.20)</td>
<td>0.0018</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.06</td>
<td>0.02</td>
<td>1.06 (1.02, 1.10)</td>
<td>0.0029</td>
</tr>
</tbody>
</table>

Paclitaxel dose forced into multivariate model
NOT a significant predictor of mortality

Significant comorbidities in patients with PAD
Comorbidities and compounding effects were NOT fully accounted for in the meta-analyses
Significant reduction in repeat revascularization with ELUVIA DES at 2 years
Fewer revascularizations leads to less patient risk, lower healthcare expenditures

Clinically-Driven TLR at 2 Years

- Year 1: 12.9%
- Year 2: 20.5%
- Year 3: 25.6%

p=0.0472
Consistent clinical benefit with ELUVIA DES in all high-risk subgroups
In Conclusion:
No Increased Mortality Risk for ELUVIA DES

- Paclitaxel is safe
- Paclitaxel-eluting coronary stents and ELUVIA DES are not included in Katsanos, VIVA, or FDA analyses
- ELUVIA DES differs from paclitaxel-coated technologies
- No observed increased mortality risk for ELUVIA DES or other paclitaxel-eluting polymeric stents
  - Long-term coronary paclitaxel-eluting experience
  - 5-year follow-up of infrapopliteal implantation (PADI)
  - ELUVIA DES results to date
In Conclusion:
No Increased Mortality Risk for ELUVIA DES

- Proven benefits of treatment with ELUVIA DES outweigh the theoretical risk
  - ~50% absolute reduction in CD-TLR at 2 years
- BSC is committed to enrollment and long-term follow-up of ongoing studies to further support safety and effectiveness of ELUVIA DES

ELUVIA DES demonstrates an excellent safety profile and consistent clinical benefit for patients with PAD
Speakers & Representatives

• Clinical Use and Data
  – Ian Meredith, MD, EVP & Global Chief Medical Officer
  – Robert A. Lookstein, MD, Professor of Radiology and Surgery, Vice Chair and Chief, Division of Interventional Radiology, Mount Sinai Medical Center

• Study Design and Conduct
  – Juan Diaz-Cartelle, MD, Senior Medical Director, Peripheral Interventions
  – Ana Becker, VP Clinical, Peripheral Interventions

• Regulatory
  – Candy Burns, VP Regulatory Affairs, Peripheral Interventions

• Device Design
  – Jay Kokate, PhD, Director R&D, Peripheral Interventions

• Statistics
  – Peter Lam, PhD, Senior Fellow, Biostatistics
Thank You