Two techniques to limit restenosis – drugs and Swirling Flow®

Or Both

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CAUTION: Investigational Device. Limited by Federal (or United States) Law to Investigational Use
Disclosure

Speaker name: Gary Ansel, MD

I have the following potential conflicts of interest to report:

- [x] Consulting Veryan Medical, Cook Medical, Medtronic, Bard
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

I do not have any potential conflict of interest
Variables That Effect Patency and Clinical Outcome

Variables

- 15-20 cm breaking point?
- Ostial
- Popliteal
- Moderate to severe or more
  - Maximized MLD
- Coagulation issues
- Technical issues
- Stent vs no stents
- Focal vs Diffuse vs Occlusion
- Drug vs no drug
12-Month Patency Rates from 3 US Pivotal DCB Trials in TASC II A-B Lesions*

- IN. PACT 360 days
- LEVANT 365 days
- ILLUMENATE 365 days

Rates based on KM Analyses
*All studies included <10%
TASC II C-D lesions
Provisional stent rates 2.2%-7.2%

N.B. Different trials with different trial characteristics
IN.PACT SFA Trial
Primary Patency Through 3 Years

Difference in CD-TLR between DCB/PTA at 3-Years was 15.9%
1. Number at risk represents the number of evaluable subjects at the beginning of each 60-day window
IN.PACT SFA Trial
Freedom from CD-TLR through 4 Years

Log-rank $P = .0399$

Schneider VIVA 17
Complex Lesions (Length, Ca++ and CTOs): The Next Hurdle for DCBs

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>LUTONIX Global</th>
<th>ILLUMENATE Global</th>
<th>IN.PACT Global Full Clinical Cohort</th>
<th>IN.PACT Global Long Lesion</th>
<th>IN.PACT Global CTO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site-reported</td>
<td>Complete follow-up</td>
<td>Interim Core Lab-adjudicated</td>
<td>1406 subjects Complete follow-up Core Lab-adjudicated</td>
<td>157 subjects Complete follow-up Core Lab-adjudicated</td>
<td>126 subjects Complete follow-up Core Lab-adjudicated</td>
</tr>
</tbody>
</table>

### Key Lesion Characteristics

<table>
<thead>
<tr>
<th>Length (cm)</th>
<th>CTO (%)</th>
<th>Ca++ (%)</th>
<th>Primary Patency FF TLR/CD-TLR</th>
<th>Bail-out Stent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.12 cm</td>
<td>31.2%</td>
<td>50.2%</td>
<td>85.4% 94.1%</td>
<td>25.2%</td>
</tr>
<tr>
<td>7.2 cm</td>
<td>28.3%</td>
<td>62%</td>
<td>86.5% 93.9%</td>
<td>15.0%</td>
</tr>
<tr>
<td>12.1 cm</td>
<td>35.5%</td>
<td>68.7%</td>
<td>92.6%</td>
<td>25.3%</td>
</tr>
<tr>
<td>26.4 cm</td>
<td>60.4%</td>
<td>71.8%</td>
<td>91.1% 94.0%</td>
<td>40.4%</td>
</tr>
<tr>
<td>22.9 cm</td>
<td>100.0%</td>
<td>71.2%</td>
<td>84.4% 88.2%</td>
<td>46.8%</td>
</tr>
</tbody>
</table>

**Note:** The data represents key lesion characteristics for Complex Lesions in terms of Length, CTO and Ca++. The table compares different global trials with their respective follow-up rates, core lab adjudication, and key lesion characteristics such as primary patency and bail-out stent usage.
Effect of calcification on DCB outcomes

DES: 5-year Primary Patency (PSVR < 2.0)

Zilver PTX vs. Standard Care

From 1-5 years, the relative separation increases by 35%

Zilver PTX

Optimal PTA + BMS

Dake et al, Circulation 2016
At 5 years, Zilver PTX demonstrates a 47% reduction in reintervention compared to BMS

Dake et al, Circulation 2016
MAJESTIC 24-Month Freedom from TLR

Kaplan-Meier Estimate

Cumulative TLR-Free Rate

96.4% (12M)
91.3% (24M)

At risk: 56 53.5 36.5

Time Post-procedure (months)
### Results

<table>
<thead>
<tr>
<th></th>
<th>Zilver BMS</th>
<th>Zilver PTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average days to TLR</td>
<td>260</td>
<td>262</td>
</tr>
<tr>
<td>Average stented length (cm)</td>
<td>15.8</td>
<td>19.1</td>
</tr>
<tr>
<td>Plaque burden (% area)*</td>
<td>28%</td>
<td>17%</td>
</tr>
</tbody>
</table>

*\(p=0.03\), statistically significant

39% relative reduction in plaque burden with Zilver PTX compared to BMS

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Ansel et al. J Endovasc Ther. 2017;24:499-503
IN.PACT Global Study
Stented vs Non-Stented Analysis
Freedom from CD-TLR Through 2 Years

Number at risk represents the number of evaluable subjects at the beginning of each 60-day window
The Need for an Improved Stent?

- N = 89, 12 death = 77 with 1 year FU
- First year of Zilver PTX use
- Cut off for short vs full length 20 cm
- Limitation of stent lengths
FULL DRUG JACKET

N = 89 (77 with 1 year FU)

At baseline Thirty-five (45.4%) of patients were in the SLG with forty-two (54.6%) in the FDJ.

Mean lesion length entire cohort was 24.2 cm (SD: 11.6; median: 24.0; range: 4.0 – 46.0)

- SLG group was = 13.3 cm ± 5.4 cm
- FDJ group = 33.2 ± 6.2 cm, p <0.001

Restenosis 1 year

- SLL group = 18.5%
- FDJ = 41.2%, p =0.058 in the FDJ.

Restenosis 2 year

- SLG = 35.3%
- FDJ = 50.0%; p=0.330

TLR 1 and 2 year

- 1 year SLG 2.9% versus FDJ 21.4%; p=0.031
- 2 year 11.4% versus FDJ 38.1% respectively, p=0.008.

Accepted and pending publication 2018 JEVT
Progress of technology

BioMimics 3D helical stent

- New generation stent
- Has all the advantages of a stent to scaffold complex disease
- Biomechanically stable in a challenging environment
- Imparts swirling flow by adding curvature to the stented segment
Swirling Flow

Vascular system uses helical curvature to promote swirling blood flow\(^1\)

Swirling Flow and Wall Shear

High wall shear protects against atherosclerosis and restenosis

SFA has naturally low wall shear

High wall shear protects against atherosclerosis and restenosis\textsuperscript{1,2}

BM3D helical stent

Computational Fluid Dynamics model of real flow from MIMICS-RCT
"This represents the first demonstration that intentionally rendering the curvature of a vessel helical to impart swirling flow improves the outcome of peripheral intervention."  

Calcium does not affect the development or effects of swirling flow.

The amount of swirling flow is the same within both minimal or severely calcified lesions.

The presence of severe calcification does not impact long term patency.

Log Rank Test
P = 0.73
### MIMICS-2: 12 MONTH DATA

#### Study Comparators

<table>
<thead>
<tr>
<th>IDE Study Device</th>
<th>DURABILITY II</th>
<th>COMPLETE SE</th>
<th>SUPERB</th>
<th>ZILVER PTX</th>
<th>IN.PACT SFA</th>
<th>IN.PACT</th>
<th>LEVANT 2</th>
<th>ILLUMENATE</th>
<th>Mimics RCT</th>
<th>BioMimics</th>
<th>MIMICS-2 BioMimics</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSVR</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.4</td>
<td>-</td>
<td>2.5</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>KM Primary Patency</td>
<td>77.2% D365</td>
<td>90.9% D360</td>
<td>92.0% D360</td>
<td>82.7% D365</td>
<td>78.4% D360</td>
<td>73.5% D365</td>
<td>82.3% D365</td>
<td>79.9% D365</td>
<td>83.2% D360</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDTLR</td>
<td>13.9% D395</td>
<td>8.4% D360</td>
<td>11.1% D390</td>
<td>9.5% D365</td>
<td>2.4% D360</td>
<td>12.3% D365</td>
<td>7.9% D410</td>
<td>8.5% D365</td>
<td>11.7% D365</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Caution: results from different trials are not necessarily comparable due to variations in enrolled populations.
MIMICS RCT: 24 MONTH DATA

Study Comparators

<table>
<thead>
<tr>
<th>IDE Study / Device</th>
<th>SUPERB / Supera</th>
<th>ZILVER PTX / Zilver PTX</th>
<th>DURABILITY II / Everflex</th>
<th>COMPLETE SE / Complete SE</th>
<th>IN.PACT SFA / IN.PACT Admiral</th>
<th>LEVANT 2 / Lutonix</th>
<th>ILLUMENATE / Stellarex</th>
<th>Mimics RCT / BioMimics 3D</th>
<th>MIMICS-2 / BioMimics 3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Occlusion</td>
<td>25%</td>
<td>30%</td>
<td>48%</td>
<td>30%</td>
<td>26%</td>
<td>21%</td>
<td>19%</td>
<td>44%</td>
<td>30%</td>
</tr>
<tr>
<td>Mod+Severe Ca^{2+}</td>
<td>44%</td>
<td>37%</td>
<td>43%</td>
<td>91%</td>
<td>8%</td>
<td>18%</td>
<td>66%</td>
<td>42%</td>
<td>46%</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>83</td>
<td>65</td>
<td>109</td>
<td>61</td>
<td>89</td>
<td>63</td>
<td>80</td>
<td>66</td>
<td>81</td>
</tr>
</tbody>
</table>

Lesion Calcification

PRIMARY PATENCY: INDEPENDENT OF CALCIFICATION

Lesion Length

PRIMARY PATENCY: INDEPENDENT OF LESION LENGTH
CONCLUSIONS

• Mimics RCT results reinforced by the larger MIMICS-2 Study

• The increase in wall shear stress is durable and continues to be effective after the point when the drug effect may be lost from either a DES or DCB

• Probability of freedom from loss of primary patency at 12 months with BioMimics 3D is similar to those for DES/DCB

• Natural Swirling Flow is an alternative to antiproliferative drugs

• Swirling flow is a natural complement to DCB for complex lesion subsets