The role of orbital atherectomy for optimization of BTK revascularization results

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Disclosure

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Potential conflicts of interest to report:
- Consulting: Silk Road, Surmodics, Profusa, CSI, Cardinal, Terumo
- Chief Medical Officer: Intact Vascular, Cagent, Vesper
- Scientific Advisory Board: Abbott, Medtronic, Boston Scientific
Orbital Atherectomy

- Manage calcification
- Create lumen space
- Change compliance
- Vessel more responsive to balloon angioplasty
- Leave healthy tissue behind
- Small particulate
Orbital Atherectomy: Mechanism of Action

- 360° crown contact designed to create a smooth, concentric lumen
- Allows constant blood flow and particulate flushing during orbit

**Differential Sanding**

Before OAS

After OAS

- Average particulate size = 2 microns
- Bi-directional sanding of superficial calcium
- Healthy elastic tissue flexes away from the crown, minimizing damage to the vessel

**Pulsatile Forces**

- Low frequency (18-40 Hz) represents crown orbit inside vessel
- High frequency (1000-1900 Hz) represents rotation of eccentric crown over the wire, producing pulsatile mechanical forces
- These pulsatile forces may affect deeper plaque and contribute to compliance change

* In a phantom non-diseased popliteal artery
** Results vary based upon plaque morphology, calcification, and anatomy
1. Based on cadaver atherosclerotic lesions, porcine coronary lesions, and graphite blocks
Orbital Atherectomy: Mechanism of Action
Centrifugal Force & Differential Sanding

Differential Sanding:
- 30 micron diamond coating for optimal “catch” of hard plaque
- Plaque provides resistance allowing diamond coating to “sand” away calcified plaque
- Healthy elastic tissue flexes away minimizing damage to the vessel

Unique Performance:
- Micro-particulate: 2 microns\(^1\)
  - RBC diameter 6-8 microns
- “No” to “Minimal” Injury in most sections after treatment with Diamondback 360° PAD System\(^1\)

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Most sections showed “No” to “Minimal” Injury After Treatment with Orbital Atherectomy.

Internal Elastic Lamina (IEL)

Media

External Elastic Lamina (EEL)

Differential Sanding Preserves Medial Integrity Demonstrated in >400 Histology Porcine Segments¹,²

2. CSI Data on file.
# Completed Prospective Peripheral Studies Focused On Calcified Lesions

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Number Patients</th>
<th># of Lesions</th>
<th>% BTK</th>
<th>% DM</th>
<th>Renal Insufficiency</th>
<th>Severe, Moderate Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>OASIS(^1)</td>
<td>124</td>
<td>201</td>
<td>86%</td>
<td>55%</td>
<td>11%</td>
<td>55%</td>
</tr>
<tr>
<td>CONFIRM I(^2)</td>
<td>733</td>
<td>1146</td>
<td>36%</td>
<td>61%</td>
<td>36%</td>
<td>76%</td>
</tr>
<tr>
<td>CONFIRM II(^2)</td>
<td>1127</td>
<td>1734</td>
<td>30%</td>
<td>60%</td>
<td>37%</td>
<td>82%</td>
</tr>
<tr>
<td>CONFIRM III(^2)</td>
<td>1275</td>
<td>1886</td>
<td>41%</td>
<td>59%</td>
<td>35%</td>
<td>83%</td>
</tr>
<tr>
<td>CALCIUM 360(^3)</td>
<td>50</td>
<td>64</td>
<td>100%</td>
<td>64%</td>
<td>24%</td>
<td>*93%</td>
</tr>
<tr>
<td>COMPLIANCE 360(^4)</td>
<td>50</td>
<td>65</td>
<td>0%</td>
<td>56%</td>
<td>N/R</td>
<td>*82%</td>
</tr>
<tr>
<td>TRUTH(^5)</td>
<td>25</td>
<td>29</td>
<td>7%</td>
<td>72%</td>
<td>24%</td>
<td>90%(^7)</td>
</tr>
<tr>
<td>LIBERTY 360(^6)</td>
<td>1204</td>
<td>1503</td>
<td>52%(^8)</td>
<td>61%</td>
<td>35%</td>
<td>44%(^9)</td>
</tr>
</tbody>
</table>

OASIS: IDE Study
CONFIRM SERIES: Real World, Complex Patients, No Exclusion Criteria
CALCIUM 360: BTK Head-to-Head Trial Comparing OAS+PTA and PTA alone
COMPLIANCE 360: ATK Head-to-Head Trial Comparing OAS+PTA and PTA alone
TRUTH: ATK IVUS Analysis
LIBERTY 360: Real World, All-Comers, All-Treatment Options PAD Study

7. Calcified (severity not specified)
8. 13% of lesions located ATK + BTK
9. Grade 3 or 4 in PACSS
Safety Profile and Complication Rates

<table>
<thead>
<tr>
<th></th>
<th>OASIS(^1) n = 201</th>
<th>CONFIRM I Diamondback(^2) n = 1146</th>
<th>CONFIRM II Predator(^2) n = 1734</th>
<th>CONFIRM III Outflow(^2) n = 1886</th>
<th>CALCIUM(^3) n = 29</th>
<th>COMPLIANCE(^4) n = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Max Inflation Pressure (atm)</td>
<td>N/R</td>
<td>5.7</td>
<td>5.4</td>
<td>5.9</td>
<td>5.9</td>
<td>4.0</td>
</tr>
<tr>
<td>Bail-out Stent due to complications</td>
<td>2.5%</td>
<td>3.8%*</td>
<td>5.8%*</td>
<td>5.2%*</td>
<td>6.9%</td>
<td>5.3%(^\ddagger)</td>
</tr>
<tr>
<td>Perforation</td>
<td>1.5%</td>
<td>0.9%</td>
<td>0.6%</td>
<td>0.7%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Embolization</td>
<td>0.5%</td>
<td>N/R</td>
<td>2.2%</td>
<td>2.2%</td>
<td>0.0%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

* Based on reported dissection treatments.
\(^\ddagger\) Adjunctive Stenting due to >30% residual stenosis

In real-world patient populations AND the most challenging lesions Orbital Atherectomy demonstrates successful lesion modification while maintaining low rates of procedural adverse events.

CONFIRM 360°: Study Design

- Prospective, multi-center registries to evaluate the use of OAS in patients with infra-inguinal PAD
- Three consecutive prospective registries conducted under common protocol from 2009 to 2011
  - Over 200 US hospitals
  - Over 350 physicians
- Real-world patients
  - No inclusion/exclusion criteria
- Three generations of OAS
  - Diamondback 360°, Predator 360°, Stealth

3,135 patients/4,766 lesions
Large PAD real-world patient data set

CONFIRM 360°: Treatment Parameters

- Average number of lesions per patient: 1.5 ± 0.8
- In most cases, 1 device was used during the procedure (1.1 ± 0.3)
- Location of the treatment and percent stenosis reduction were similar across CONFIRM series
  - Slight trend toward higher BTK utilization in CONFIRM III
  - Post OAS residual stenosis 35 ± 19%
  - Final residual stenosis 10 ± 11%

Multi vessel (e.g., ATK + BTK): ~20%

Prospective, multi-center, acute registries to evaluate the use of OAS in patients with infra-inguinal PAD (n=4,766 lesions)

Evolution of Safety Profile Based on Compliance Change in CONFIRM 360° Series

% Procedural Complications

CONFIRM I vs II (p<0.001)
CONFIRM I vs III (p<0.001)

CONFIRM I vs II (p<0.001)
CONFIRM I vs III (p<0.001)

CONFIRM I vs II (p=0.04)
CONFIRM I vs III (p=0.13)

Prospective, multi-center, acute registries to evaluate the use of OAS in patients with infra-inguinal PAD (n=4,766 lesions)

Overall CONFIRM Procedural Outcomes

<table>
<thead>
<tr>
<th>Per Lesion</th>
<th>CONFIRM I n = 1146</th>
<th>CONFIRM II n = 1734</th>
<th>CONFIRM III n = 1886</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Max Inflation</td>
<td>5.7 atm</td>
<td>5.4 atm</td>
<td>5.9 atm</td>
</tr>
<tr>
<td>Bail-Out Stent (due to dissections)</td>
<td>3.8%</td>
<td>5.8%</td>
<td>5.2%</td>
</tr>
<tr>
<td>Perforation</td>
<td>0.9%</td>
<td>0.6%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>N/R</td>
<td>2.2%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Vessel closure</td>
<td>2.1%</td>
<td>1.2%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

OAS consistently demonstrates plaque modification with
- Low inflation pressure
- Low bail out stent rates
- Low procedural events

## CONFIRM Series – Sub-analyses – Acute Complication Rates

<table>
<thead>
<tr>
<th></th>
<th>Age&lt;75 (n=1,753)</th>
<th>Age≥75 (n=1,242)</th>
<th>P</th>
<th>Women (n=1,261)</th>
<th>Men (n=1,870)</th>
<th>p</th>
<th>DM (n=1,842)</th>
<th>No DM (n=1,247)</th>
<th>p</th>
<th>Renal disease (n=1,105)</th>
<th>No renal disease (n=1,969)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow-limiting dissection</td>
<td>1.6%</td>
<td>1.5%</td>
<td>0.51</td>
<td>1.6%</td>
<td>1.4%</td>
<td>0.61</td>
<td>1.5%</td>
<td>1.4%</td>
<td>0.81</td>
<td>1.3%</td>
<td>1.7%</td>
<td>0.39</td>
</tr>
<tr>
<td>Perforation</td>
<td>0.4%</td>
<td>1.2%</td>
<td>0.01</td>
<td>0.8%</td>
<td>0.7%</td>
<td>0.57</td>
<td>0.5%</td>
<td>1.1%</td>
<td>0.03</td>
<td>0.6%</td>
<td>0.8%</td>
<td>0.55</td>
</tr>
<tr>
<td>Slow flow</td>
<td>4.0%</td>
<td>5.3%</td>
<td>0.08</td>
<td>4.4%</td>
<td>4.5%</td>
<td>0.96</td>
<td>5.0%</td>
<td>3.5%</td>
<td>0.02</td>
<td>5.0%</td>
<td>4.2%</td>
<td>0.19</td>
</tr>
<tr>
<td>Closure</td>
<td>1.7%</td>
<td>1.1%</td>
<td>0.13</td>
<td>1.8%</td>
<td>1.2%</td>
<td>0.11</td>
<td>1.7%</td>
<td>0.9%</td>
<td>0.06</td>
<td>1.1%</td>
<td>1.6%</td>
<td>0.08</td>
</tr>
<tr>
<td>Spasm</td>
<td>6.3%</td>
<td>6.4%</td>
<td>0.96</td>
<td>6.8%</td>
<td>6.0%</td>
<td>0.24</td>
<td>5.5%</td>
<td>7.6%</td>
<td>0.005</td>
<td>6.7%</td>
<td>6.2%</td>
<td>0.40</td>
</tr>
<tr>
<td>Embolism</td>
<td>2.5%</td>
<td>1.6%</td>
<td>0.31</td>
<td>2.8%</td>
<td>1.9%</td>
<td>0.07</td>
<td>2.2%</td>
<td>2.4%</td>
<td>0.67</td>
<td>1.7%</td>
<td>2.6%</td>
<td>0.12</td>
</tr>
<tr>
<td>Thrombus</td>
<td>1.6%</td>
<td>0.9%</td>
<td>0.03</td>
<td>1.3%</td>
<td>1.2%</td>
<td>0.74</td>
<td>1.3%</td>
<td>1.1%</td>
<td>0.75</td>
<td>1.4%</td>
<td>1.0%</td>
<td>0.56</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Office based lab</th>
<th>CLI/Claudicant</th>
<th>CLI ATK vs. BTK lesions</th>
<th>Complication rates</th>
<th>Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>1.5%</td>
<td>0.0%</td>
<td>0.30</td>
<td>RC 1-3 (n=1,697)</td>
<td>1.4%</td>
</tr>
<tr>
<td>OBL</td>
<td>0.1%</td>
<td>0.0%</td>
<td>0.98</td>
<td>RC 1-3 (n=1,697)</td>
<td>0.6%</td>
</tr>
<tr>
<td>p</td>
<td>4.6%</td>
<td>0.0%</td>
<td>0.19</td>
<td>RC 1-3 (n=1,697)</td>
<td>2.9%</td>
</tr>
<tr>
<td>Perforation</td>
<td>1.4%</td>
<td>2.8%</td>
<td>0.11</td>
<td>RC 1-3 (n=1,697)</td>
<td>1.4%</td>
</tr>
<tr>
<td>Slow flow</td>
<td>6.4%</td>
<td>3.7%</td>
<td>0.58</td>
<td>RC 1-3 (n=1,697)</td>
<td>3.8%</td>
</tr>
<tr>
<td>Closure</td>
<td>2.3%</td>
<td>0%</td>
<td>0.32</td>
<td>RC 1-3 (n=1,697)</td>
<td>1.7%</td>
</tr>
<tr>
<td>Spasm</td>
<td>1.2%</td>
<td>1.9%</td>
<td>0.17</td>
<td>RC 1-3 (n=1,697)</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

*P-values form adjusted logistic regression

Patency at 12 Months

- OAS + PTA (n=32 lesions): 81.2%
- PTA ALONE (n=23 lesions): 78.3%

Similar patency despite large difference in stents placed

Patency definition: Freedom from TLR or restenosis (Peak Systolic Velocity Ratio (PSVR) ≥2.5)

ORBITAL AHERECTOMY SYSTEM DEMONSTRATED REDUCED STENTING WITH DURABLE RESULTS OUT TO 12 MONTHS VS. PTA ALONE

Prospective, randomized, multi-center study that compared acute and long-term results of OAS+PTA and PTA alone in calcified ATK lesions

Mean Max Balloon Pressure (atm)

- OAS + PTA (n=38): 4.0 atm
- PTA ALONE (n=27): 9.1 atm

p < 0.001

Adjunctive Stenting

- OAS + PTA (n=38): 5.3%
- PTA ALONE (n=27): 77.8%

p < 0.001
CALCIUM 360°: Results

Prospective, randomized, multi-center study that compared acute and long-term results of OAS+PTA and PTA alone in calcified BTK lesions.

### Results at 12 Months

<table>
<thead>
<tr>
<th></th>
<th>Freedom From Revascularization</th>
<th>Freedom From Major Adverse Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>OAS + PTA</strong></td>
<td>93.3%</td>
<td>93.3%</td>
</tr>
<tr>
<td>n=15 patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PTA ALONE</strong></td>
<td>80.0%</td>
<td>57.9%</td>
</tr>
<tr>
<td>n=15 patients</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MAE (major adverse events: device- or procedure-related major amputation (above the ankle), all-cause mortality and TLR/TVR).

Liberty 360-1204 patients
18-Month Freedom from MAE and Amputation Free Survival

High freedom from MAE in all groups with similar MAE outcomes in RC4-5 and RC6. High freedom from major amputation in all Rutherford Classes (RC2-3, 100%; RC4-5, 95.3%; and RC6, 91.3%).

18-Month Freedom from MAE – OAS

<table>
<thead>
<tr>
<th>Rutherford 2-3</th>
<th>At Risk</th>
<th>127</th>
<th>Events</th>
<th>36</th>
<th>Censored</th>
<th>51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutherford 4-5</td>
<td>At Risk</td>
<td>97</td>
<td>Events</td>
<td>59</td>
<td>Censored</td>
<td>77</td>
</tr>
<tr>
<td>Rutherford 6</td>
<td>At Risk</td>
<td>25</td>
<td>Events</td>
<td>17</td>
<td>Censored</td>
<td>14</td>
</tr>
</tbody>
</table>

FF Major Amputation 18-Month Rates – OAS

| Rutherford 2-3 | 100.0% |
| Rutherford 4-5 | 95.3%  |
| Rutherford 6   | 91.3%  |

FF TVR

| Rutherford 2-3 | 81.6%  |
| Rutherford 4-5 | 74.2%  |
| Rutherford 6   | 70.7%  |

FF All Death*

| Rutherford 2-3 | 94.9%  |
| Rutherford 4-5 | 86.5%  |
| Rutherford 6   | 82.9%  |

Amputation Free Survival

| Rutherford 2-3 | 94.9% |
| Rutherford 4-5 | 82.5% |
| Rutherford 6   | 75.1% |

**MAE rate differences assessed via Cox Proportional Hazards model [MAE: Death to 30 days, Major amputation, TVR]. Kaplan-Meier method used to obtain estimate rates. Greenwood’s method used to obtain the 95% confidence interval for the estimate. 30-Oct-2017 Data**

**FF = Freedom From. * All Death rate shown here is at 18 months, but the Freedom from MAE (shown on left) only includes death within 30-days of the procedure. Amputation free survival defined as freedom from death and target limb major amputation.**
Obital Atherectomy

Conclusion

• Excellent procedural safety.
• Unique mechanism for managing tibial calcification.
• More responsive to angioplasty.
The role of orbital atherectomy for optimization of BTK revascularization results

Peter A. Schneider, MD
Honolulu, Hawaii