Pivotal Trial to Evaluate the Safety and Efficacy of the Diamondback 360° Orbital Atherectomy System in Treating *De Novo*, Severely Calcified Coronary Lesions (ORBIT II)

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Severe Coronary Calcium is Under Estimated and Under Appreciated

- Despite being a relatively common problem there have been no FDA IDE PMA trials studying only patients with severe coronary calcification.

- Due to poor clinical outcomes, including higher MACE and angiographic complications, patients with severe calcium have been excluded from almost all large scale clinical trials.
Complications

• Calcified Lesions
  - Prone to dissection during balloon angioplasty or pre-dilatation\(^1\)
  - Difficult to completely dilate\(^2\)
  - Can prevent adequate stent expansion\(^3\)
  - Preclude stent delivery to the desired location\(^4\)

Outcomes in Calcified Lesions
Unstudied population

<table>
<thead>
<tr>
<th>Publication</th>
<th>Severe Calcium / Total Pts</th>
<th>Type of Calcification Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dill Eur Heart J, 2000</td>
<td>98 / 249</td>
<td>Calcified</td>
</tr>
<tr>
<td>Safian CCI, 2001</td>
<td>54 / 254</td>
<td>Calcified</td>
</tr>
<tr>
<td>Doshi AJC, 2003</td>
<td>557 / 843</td>
<td>Moderate/severe</td>
</tr>
<tr>
<td>Mosseri CRM, 2005</td>
<td>75 / 540</td>
<td>Severe</td>
</tr>
<tr>
<td>Clavijo CCI, 2006</td>
<td>81 / 81</td>
<td>Heavy</td>
</tr>
</tbody>
</table>

Note: Includes retrospective data and lack of core lab adjudication

Weighted Average Procedural Success = 84%
Weighted MACE Rate at 30 days = 15.9%
Pivotal Trial to Evaluate the Safety and Efficacy of the
Diamondback 360° Orbital Atherectomy System in
Treating De Novo, Severely Calcified Coronary Lesions
Orbital Technology for Calcified Coronary Arteries

- Easy setup and use
- Control of device in operating field
- .012” OAS guide wire
- Compatible with 6 French guiding catheters

Eccentric Crown

ViperWire™

Electric OAS

Caution – Investigational Device. Limited by Federal (or United States) law to investigational use.
Unique Mechanism of Action
Differential Orbital Sanding

Crown will only sand the hard components of plaque

Soft components (plaque/tissue) flex away from crown

Orbital Mechanism

• Increased speed = Increased centrifugal force
• Greater centrifugal force = Larger orbital diameter

\[ CF = \text{Mass} \times \text{Rotational speed}^2 \]
Radius of the orbit

Actual results may vary depending on device-to-lumen ratio, run time and speed, and plaque morphology.
Unique Mechanism of Action

• Orbiting Crown Enables
  • Continuous flow of blood and saline
    • Minimizes thermal injury
    • Potentially decreases no-reflow and periprocedural cardiac enzyme elevation
  • One crown treats different vessel diameters based on orbiting speed

Actual results may vary depending on device-to-lumen ratio, run time and speed, and plaque morphology.
Coronary OAS Mechanism Of Action

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ORBIT II Study Design

- To evaluate safety and efficacy of coronary OAS to prepare *de novo* severely calcified coronary lesions for enabling stent placement
  - Prospective
  - Multi-center trial
  - Single arm - FDA recommendation as there are no FDA-approved percutaneous treatments for patients with severely calcified lesions.

443 patients enrolled in 49 US sites

30 days follow-up

Complete in 97.7% (N=430/440)
The ORBIT II Trial: Primary Endpoints

Primary Safety Endpoint: 30-Day MACE

- MI defined as CK-MB level > 3 times ULN
- Target vessel revascularization (TVR)
- Cardiac death

Primary Efficacy Endpoint: Procedural Success

- Success in facilitating stent delivery with a final residual stenosis of <50% and without in-hospital MACE

In Hospital MACE Impacts Both Primary Endpoints

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Inclusion Criteria

- The target lesion must be a *de novo* coronary lesion that has not been previously treated with any interventional procedure.
- The target vessel reference diameter must be $\geq 2.5\text{mm}$ and $\leq 4.0\text{mm}$.
- The target lesion must not exceed $40\text{mm}$.
- The target vessel must have a TIMI 3 flow at baseline.
- The target lesion must have fluoroscopic or IVUS evidence of severe calcium deposit at the lesion site based on the protocol definition.

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**ORBIT II Severe Calcification Definition:**

*Only Includes The Most Severely Calcified Lesions*

**Mintz\(^1\) 1995 calcium definition**

- **Moderate**: radiopacities noted only during the cardiac cycle before contrast injection
- **Severe**: radiopacities noted without cardiac motion before contrast injection generally compromising both sides of the arterial lumen

**ORBIT II Severe Calcium**

- Presence of radiopacities noted without cardiac motion prior to contrast injection involving both sides of the arterial wall in at least one location.
- Total length of calcium (including segmented) must be at least 15 mm and extend partially into the target lesion
- OR presence of \( \geq 270^\circ \) of calcium at one cross section via IVUS

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Exclusion Criteria

- Diagnosed with chronic renal failure unless under hemodialysis, or has a serum creatinine level >2.5 mg/dl.
- Evidence of current LVEF ≤25% (where current is defined as the latest LVEF measurement completed within the last 6 months).
- Subject with angiographically confirmed evidence of more than 1 lesion requiring intervention, unless the treatment of the lesions is staged.
- Target vessel has a stent from previous PCI unless 1) the stent was implanted greater than 30 days prior to the index procedure, and 2) the stent has no higher than 30% in-stent stenosis, and 3) the stent is on a different branch than the target lesion.
- Target lesion is an ostial location (within 5 mm of ostium) or an unprotected left main lesion.
- Target lesion is a bifurcation or has a ≥ 1.5 mm side branch.
- Target lesion has thrombus or dissection.
## ORBIT II: Demographics & Characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>64.6%</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>71.4</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>36.2%</td>
</tr>
<tr>
<td>History of CABG</td>
<td>14.7%</td>
</tr>
<tr>
<td>History of dislipidemia</td>
<td>91.9%</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>91.6%</td>
</tr>
<tr>
<td>Smoker (current or previous)</td>
<td>66.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vessel &amp; Lesion Characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pre-procedure target lesion length</td>
<td>18.9 mm</td>
</tr>
<tr>
<td>Mean pre-procedure percent stenosis</td>
<td>84.4%</td>
</tr>
<tr>
<td>IVUS degree of calcium (35/440, 8%)</td>
<td>270-360°</td>
</tr>
</tbody>
</table>

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ORT II: Primary Safety Endpoint

30 Day MACE Rate Components:

- MI (CK-MB >3x ULN):
  - Non Q-wave: 8.8%
  - Q-wave: 0.9%

- TVR/TLR:
  - TVR: 0.7%
  - TLR: 0.7%

- Cardiac death: 0.2%

**Performance Goal = 83%**

**Freedom from 30 Day MACE = 89.8%**

(95% CI = 87.0%, 92.7%)
ORBIT II: Primary Efficacy Endpoint

Procedural Success Components:

- Successful Stent delivered: 97.7%
- Less than 50% residual stenosis: 98.6%
- In hospital MACE: 9.5%
  - MI (CK-MB >3x ULN):
    - Non Q-wave: 8.6%
    - Q-wave: 0.7%
  - TVR: 0.7%
- Cardiac death: 0.2%

Performance Goal = 82%

Procedural Success = 89.1%

95% CI = 85.8%, 91.8%
Non Q Wave MI in Severely Calcified Lesions

Mosseri (2005)\(^1\)

Mintz 1995 calcium definition

\[ n = 662 \]

Increasing calcium deposits increases the incidence of non Q-wave MI

- 0-90°: 8.0%
- 91-180°: 9.8%
- 181-270°: 12.3%
- 271-360°: 20.9%

Clavijo (2006)\(^2\)

Mintz 1995 calcium definition

\[ n = 150 \]

- SES: 25.8%
- RA+SES: 19.8%

ORBIT II

Orbit II calcium definition

\[ n = 443 \]

- OAS+DES/BMS: 8.6%

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Death Rates in Severely Calcified Lesions


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ORBIT I Trial

- First-in-man study using orbital atherectomy in coronary arteries
- Designed to demonstrate safety and performance in calcified coronary lesions
  - Prospective, single-arm
  - 2 centers OUS
  - 50 subjects with >90° of calcium via IVUS
- Compared to ORBIT II
  - Shorter lesions
  - Less B2/C lesions

<table>
<thead>
<tr>
<th>MACE rate</th>
<th>30 days¹</th>
<th>6 months¹</th>
<th>2 years²</th>
<th>3 years²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3/50 (6%)</td>
<td>4/50 (8%)</td>
<td>5/33 (15%)</td>
<td>6/33 (18.2%)</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>2 (6%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Non Q-wave MI</td>
<td>3 (6%)</td>
<td>3 (6%)</td>
<td>3 (9%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>TLR</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>


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Female, 70 years old

History of DM, smoker, dyslipidemia, HTN, EF 50%, Positive stress test

Lesion length 24 mm
ORBIT II Case Studies: LCX (Treatment)

1.25 mm Crown
With Electric OAD

Low Speed, 15 Seconds

High Speed, 15 Seconds

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ORBIT II Case Studies: LCX (Final)
Single DES

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Conclusion

- The ORBIT II trial was unique in enrolling only patients with severely calcified coronary arteries.
- The ORBIT II trial met the primary safety and efficacy endpoints by a significant margin.
- There was a decrease in the incidence of MACE (mortality, MI and TVR) in comparison to the historical controls when this device was used.
- The improvement in clinical outcome might be attributed to the unique mechanism of action of OAS.
- OAS is a technology that may address an unmet treatment need for this difficult to treat patient population.