Shockwave Medical Lithoplasty®

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Disclosure

Speaker name: Thomas Zeller, MD

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest
**Problem:** Rigid fibrotic, calcified tissue

Today’s endovascular therapies fail

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**Current Cycle of Therapy**

1. **High Pressure Inflation**
   - Wall Stress

2. **Restenosis**
   - Revascularization failure

3. **Injury**
   - Disrupts IEL

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Lithoplasty®

Lesion modification pre-dilation using lithotripsy in a balloon

- Designed to normalize vessel wall compliance prior to controlled, low pressure dilatation
- Effective lesion expansion with minimized impact to healthy tissue
- Familiar Balloon-based endovascular technique
- “Front-line” balloon strategy (.014”compatible)

Tissue-selective: Hard on hard tissue, Soft on soft tissue

Lithotripsy waves travel outside balloon

Designed to disrupt both superficial, deep calcium

The Lithoplasty System holds CE Marking for lithotripsy-enhanced, low-pressure balloon dilation of calcified, stenotic peripheral arteries in patients who are candidates for percutaneous therapy. Not available for sale in the US.
DISRUPT PAD 1 Study

Inclusion Criteria
- Rutherford II-IV Intermittent Claudication (n= 35 Patients)
- ABI < 0.9
- SFA/Popliteal Lesion > 70% stenosis, 3.3-7.0 mm, < 180 mm
- Screen CT, MR, X-ray
- Angiographic Moderate/Severe Calcification

Procedure
- Lithoplasty 3.5 to 7.0 x 60 mm Multi-electrode Balloon

Endpoints
- Acute Angiographic Result-Core lab adjudicated
- Duplex Ultrasound 30 & 180 Days-Core lab adjudicated
- Safety-30 day MAE-CEC Adjudicated
DISRUPT PAD 1 (35 pts./39 lesions): Performance Outcomes

**Procedural Success:**
- Residual stenosis <50% with or without adjunctive PTA
- < 50% Residual stenosis - 100%
- ≤ 30% Residual stenosis - 87%
- Average residual stenosis - 23%
- Stents – 0%

**6 month Outcomes:**
- 83% patency and no TLRs in moderate and severe calcium

<table>
<thead>
<tr>
<th></th>
<th>Patency Rate</th>
<th>TLR Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge</td>
<td>97%</td>
<td>0%</td>
</tr>
<tr>
<td>30 Day</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>6 Month</td>
<td>83%</td>
<td>0%</td>
</tr>
</tbody>
</table>

* Patency defined as <50% restenosis (PSVR ≤2.5)
DISRUPT PAD 1: Safety

• No Major Adverse Events through primary endpoint at 30 days or out to 6 months

<table>
<thead>
<tr>
<th>Event</th>
<th>30 days N=35</th>
<th>6 months N=35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for emergency surgical revascularization of target limb</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Unplanned target limb amputation (above the ankle)</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Symptomatic thrombus or distal emboli (^1)</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Perforations and dissections of grade D or greater that require an intervention to resolve, including bail-out stenting</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*All events adjudicated by independent Clinical Events Committee
1 Defined as clinical signs or symptoms of thrombus or distal emboli detected in the treated limb in the area of the treated lesion or distal to the treated lesion after the index procedure or noted angiographically, and requiring mechanical or pharmacologic means to improve flow
Pre-procedure:

- DS = 100%
- Lesion Length = 76.5 mm

Calcification:

- Total Length of Ca = 74.8 mm

Lithoplasty Balloon:

- Prox. RVD = 5.50 mm
- Dist. RVD = 6.05 mm
- Interpolated RVD = 5.89 mm
- MLD = 4.59 mm
- DS % = 21.94%

Final:

- Core Lab Residual: 22%
- 27.5 mm OL

- Prox. RVD = 5.50 mm
- Dist. RVD = 6.05 mm
- Interpolated RVD = 5.89 mm
- MLD = 4.59 mm
- DS % = 21.94%
Inclusion Criteria

• Rutherford II-IV Intermittent Claudication (n= 60 Patients)
• ABI < 0.9
• SFA/Popliteal Lesion > 70% stenosis, 3.3-7.0 mm, < 180 mm
• CTO (up to 8 cm)
• Angiographic Moderate/Severe Calcification

Procedure

• Lithoplasty 3.5 to 7.0 x 60 mm Multi-electrode Balloon

Endpoints

• Primary
  • Safety-30 day MAE-CEC Adjudicated
  • Efficacy -12 month patency (DUS)
• Secondary
  • Efficacy-Acute Angiographic Result-Core lab adjudicated; 30& 180 day patency & TLR; Clinical (ABI, pain, walking distance)
# Investigative Sites

60 patients enrollment completed (Dec 2015)

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Site</th>
<th>Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marianne Brodmann, MD</td>
<td>Universitätsklinikum LKH Graz</td>
<td>15</td>
</tr>
<tr>
<td>Martin Werner, MD</td>
<td>Hanusch Krankenhaus</td>
<td>14</td>
</tr>
<tr>
<td>Florian Wolf, MD</td>
<td>Medical University of Vienna</td>
<td>1</td>
</tr>
<tr>
<td>Thomas Zeller, MD (PI)</td>
<td>Universitäts-Herzzentrum Freiburg &amp; Bad Krozingen</td>
<td>10</td>
</tr>
<tr>
<td>Gunnar Tepe, MD</td>
<td>RoMed Klinikum Rosenheim</td>
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</tr>
<tr>
<td>Giovanni Torsello, MD</td>
<td>St. Franziskus Hospital/Universitätsklinikum Münster</td>
<td>1</td>
</tr>
<tr>
<td>Dierk Sheinert, MD</td>
<td>University Leipzig Medical Centre</td>
<td>3</td>
</tr>
<tr>
<td>Andrew Holden, MD</td>
<td>Auckland City Hospital</td>
<td>6</td>
</tr>
</tbody>
</table>
PAD 2: Acute Procedural Success

Results continue to be consistent with PAD 1

**Procedural Success:** N= 57 (60 lesions) analyzed
- Residual stenosis <50% with or without adjunctive PTA
- Primary Endpoint < 50% Residual stenosis: 100%
- Exploratory Endpoint ≤ 30% Residual stenosis: 91%
- Stents: 1.7%

% Diameter Stenosis, Pre and Post  (core lab adjudicated)
PAD 2: Angiographic Outcomes

<table>
<thead>
<tr>
<th>Pre-procedure</th>
<th>N = 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVD (mm)</td>
<td>5.39 ± 0.78</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.17 ± 0.72</td>
</tr>
<tr>
<td>Diameter stenosis %</td>
<td>77.75 ± 13.00</td>
</tr>
<tr>
<td>CTO</td>
<td>9 (16%)</td>
</tr>
<tr>
<td>Lesion length</td>
<td>76 ± 37.5</td>
</tr>
<tr>
<td>Calcium</td>
<td>Moderate: 29 (51%)</td>
</tr>
<tr>
<td></td>
<td>Severe: 28 (49%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-procedure</th>
<th>N = 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD (mm)</td>
<td>4.15 ± 0.58</td>
</tr>
<tr>
<td>Diameter stenosis %</td>
<td>24.36 ± 5.70</td>
</tr>
<tr>
<td>Acute gain (mm)</td>
<td>2.98 ± 0.80</td>
</tr>
<tr>
<td>Dissection</td>
<td>None: 48 (84%)</td>
</tr>
<tr>
<td></td>
<td>A: 0</td>
</tr>
<tr>
<td></td>
<td>B: 5 (9%)</td>
</tr>
<tr>
<td></td>
<td>C: 4 (7%)</td>
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</tbody>
</table>

No post-procedure angiographic complications including thrombus, spasm, acute closure, distal embolization or perforations
Summary

- Lithoplasty® is safe and effective in the treatment of calcified SFA/Popliteal lesions
- “Stent like” acute result without an implant
- 6-month durability in DISRUPT PAD:
  - 83% patency
  - 0% TLR
- Consistent DISRUPT PAD 2 acute success with limited angiographic complications
- 12-month patency Q4 2016

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