Is combination therapy with directional atherectomy followed by DCB the answer to challenges in treating SFA disease? The REALITY trial

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Disclosure

Speaker name:
G. Torsello

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
Factors associated with restenosis in peripheral interventions

- Lesion length\(^1\)
- Diabetes\(^2\)
- Occlusions\(^3\)
- Calcification\(^4\)

DCB is a proven technology in TASC A & B lesions

3-year outcomes from the IN.PACT SFA RCT

However, outstanding outcomes seen in global registries come at the cost of high bailout stenting rates. *The longer the lesion, the higher the bailout stent rate*.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>LUTONIX Global(^1)</th>
<th>ILLUMINATE Global(^2)</th>
<th>IN.PACT Global Full Clinical Cohort(^3)</th>
<th>IN.PACT Global Long Lesion(^4)</th>
<th>IN.PACT Global CTO(^5)</th>
<th>IN.PACT Global ISR(^6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>691 subjects</td>
<td></td>
<td></td>
<td>1406 subjects</td>
<td>157 subjects</td>
<td>126 subjects</td>
<td>131 subjects</td>
</tr>
<tr>
<td>Complete follow-up</td>
<td></td>
<td></td>
<td>Interim Core Lab-adjudicated</td>
<td>Complete follow-up Core Lab-adjudicated</td>
<td>Complete follow-up Core Lab-adjudicated</td>
<td>Complete follow-up Core Lab-adjudicated</td>
</tr>
<tr>
<td>Site-reported</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

#### Key Lesion Characteristics

<table>
<thead>
<tr>
<th>Length (cm)</th>
<th>CTO (%)</th>
<th>Ca(^{2+}) (%)</th>
<th>Primary Patency</th>
<th>FF TLR/CD-TLR</th>
<th>Bail-out Stent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.12cm</td>
<td>31.2%</td>
<td>50.2%</td>
<td>85.4%</td>
<td>94.1%</td>
<td>25.2%</td>
</tr>
<tr>
<td>7.2cm</td>
<td>28.3%</td>
<td>62%</td>
<td>86.5%</td>
<td>93.9%</td>
<td>15.0%</td>
</tr>
<tr>
<td>12.1cm</td>
<td>35.5%</td>
<td>68.7%</td>
<td>91.1%</td>
<td>92.6%</td>
<td>25.3%</td>
</tr>
<tr>
<td>26.4cm</td>
<td>60.4%</td>
<td>71.8%</td>
<td>94.0%</td>
<td>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%</td>
<td>88.2%</td>
<td>46.8%</td>
</tr>
<tr>
<td>17.2 cm</td>
<td>34.0%</td>
<td>59.1%</td>
<td>88.7%</td>
<td>92.9%</td>
<td>14.5%</td>
</tr>
</tbody>
</table>

Primary patency & late lumen loss negatively impacted by increasingly severe calcification

Studies have shown Ca\(^{++}\) represents a barrier to optimal drug absorption

IN.PACT DCB and Calcium Registry Study (n=60) 12 month Results\(^1\)

- Retrospective analysis of 91 patients\(^2\)
- Analysed at 6M post DEB
- Lesion calcification analysed by core labs (PACSS score + angiographic calcium score)
- Severity of lesion calcification is associated with LLL after treatment with DCB.
- Author conclusion: “One possible approach to overcome this limitation might be plaque modification or removal prior to DEB usage.”

Why combination of atherectomy and drug elution?

1. Sufficient luminal gain
2. Reduce calcium burden
3. Increase paclitaxel bioavailability
4. Bailout stenting reduction
5. Inflammation reduction after debulking

After Atherectomy

After DCB

Long-Severely Calcified Lesion
Which device?

- Ability to remove calcified plaque
- Generate significant lumen gain
- Favourable complication profile

12 Month Patency

<table>
<thead>
<tr>
<th>Device</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CELLO (Laser)</td>
<td>65</td>
<td>54%</td>
</tr>
<tr>
<td>Pathway PVD (JetStream)</td>
<td>172</td>
<td>62%</td>
</tr>
<tr>
<td>DEFINITIVE LE (DA)</td>
<td>N</td>
<td>78%</td>
</tr>
</tbody>
</table>

DEFINITIVE Ca++ demonstrated calcified disease can be treated with DA and embolic protection

**DEFINITIVE LE and Ca\(^{2+}\): Outcomes**

_SilverHawk, TurboHawk (Medtronic)_

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Patient #</td>
<td>598 (RCC 1-3)</td>
<td>201 (RCC 4-6)</td>
</tr>
<tr>
<td>Lesion #</td>
<td>743</td>
<td>279</td>
</tr>
<tr>
<td>Bail-out Stent</td>
<td>3.2% (33/1022)</td>
<td>4.1% (7/169)(^1)</td>
</tr>
<tr>
<td>MAE (30d)</td>
<td>1.0% (6/598)</td>
<td>3.5% (7/201)</td>
</tr>
<tr>
<td>1(^{o}) Patency (1y)</td>
<td>78.0%</td>
<td>71.0%</td>
</tr>
<tr>
<td>1(^{o}) Patency Def</td>
<td>PSVR ≤ 2.4 by DUS</td>
<td>NR(^2)</td>
</tr>
<tr>
<td>TLR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR = Not Reported. Boldfaced values indicate statistical significance (p < 0.05).

1. Site-reported lesions totaled 169 while Core Lab evaluated lesions totaled 168 (two site-reported lesions were considered one diffuse lesion by the Core Lab). Provisional stent rate was reported by Roberts, et al., with respect to the site-reported lesion number, i.e. 169 not 168.
2. Primary endpoint for DEFINITIVE Ca\(^{2+}\) was safety; patency was not evaluated.

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DEFINITIVE AR\(^1\)

Pilot study to detect trends in treatment differences between groups and designed to assess the effect of treating lesions with DA followed by DCB (DAART)

**DAART: Directional Atherectomy + Anti-Restenotic Therapy**

**Inclusion Criteria**
- RCC 2-4
- \(\geq 70\%\) stenosis of SFA and/or popliteal artery
- Lesion Length 7-15cm
- Reference Vessel \(\geq 4\)mm and \(\leq 7\)mm

**Exclusion Criteria**
- In-stent restenosis
- Aneurysmal target vessel
- Multiple lesions in target limb that require treatment

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DEFINITIVE AR 1 Year Outcomes

Emerging advantage in long & severely calcified lesions

The REALITY Study evaluates patient outcomes with adjunctive use of Medtronic HawkOne™ or Medtronic TurboHawk™ and Medtronic IN.PACT™ Admiral™ drug-coated balloon.

- The multi-center, international, prospective, single-arm study will enroll up to 250 subject at up to 15 sites.
- The study includes angiographic and duplex ultrasound core lab adjudication. Primary patency is assessed by duplex ultrasound at 12-months.
- Patients are followed up to 24 months to determine clinically driven target lesion revascularization (CD-TLR).
- The study is sponsored and managed by VIVA physicians with support from Medtronic through an external research project grant.

ClinicalTrials.gov Identifier: NCT02850107
Primary Effectiveness Endpoint:
Primary patency (PSVR ≤ 2.4) and freedom from CD-TLR at one-year in subjects with long, moderate and severely calcified symptomatic femoropopliteal lesions and/or occlusions after treatment with DA + DCB.

Primary Safety Endpoint:
Freedom from (MAEs) defined as freedom from flow-limiting dissections (D-F), vessel perforations requiring stenting or stent-grafts, unplanned amputation, intra-procedure distal atheroembolization and clinically-driven TVR in subjects with long, moderate and severely calcified FP lesions and/or occlusions through 30-day follow-up visit.

ClinicalTrials.gov Identifier: NCT02850107
I have a dream!
I have a dream as vascular specialist too

- Increase the applicability of endovascular techniques also in patients with complex lesions
- Including patients with limited number of runoff vessels, with severe lower limb ischemia and diabetes
- Improve long term patency also for long/calcified lesions
Conclusions

• Directional atherectomy and DCB perform well as standalone treatments
• Early data suggests that combined therapy may improve patient outcomes in more complex lesions
• REALITY will show whether DAART is the right answer to challenges in treating SFA disease
Thank you!
Is combination therapy with directional atherectomy followed by DCB the answer to challenges in treating SFA disease? The REALITY trial

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