Present State of Atherectomy Devices for Lower Limb Ischemia: How Solid is the Evidence That They Make a Difference: A Surgeon’s View

VEITH 2015

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DEFINITIVE LE
Key Eligibility Criteria

Inclusion Criteria
- RCC 1-6
- ≥ 50% stenosis
- Lesion Length ≤ 20 cm
- Reference Vessel ≥ 1.5 mm and ≤ 7.0 mm

Exclusion Criteria
- Severe calcification
- In-stent restenosis
- Aneurysmal target vessel

Study Design and Primary Endpoints

800 patients
47 centers
Claudicants (RCC 1-3)
598 patients*
Primary patency by Duplex US at 12 mos

CLI (RCC 4-6)
201 patients
Freedom from major unplanned amputation at 12 mos

*1 censored due to informed consent violation

Baseline Lesion Characteristics
Core Lab Reported

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Claudication (RCC 1-3)</th>
<th>CLI (RCC 4-6)</th>
<th>All Subjects (RCC 1-6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>598</td>
<td>201</td>
<td>799</td>
</tr>
<tr>
<td>Number of Lesions</td>
<td>743</td>
<td>279</td>
<td>1022</td>
</tr>
<tr>
<td>Mean Length (cm)</td>
<td>7.5</td>
<td>7.2</td>
<td>7.4</td>
</tr>
<tr>
<td>Baseline Stenosis (%)</td>
<td>73</td>
<td>76</td>
<td>74</td>
</tr>
<tr>
<td>Occlusions (%)</td>
<td>17</td>
<td>30</td>
<td>21</td>
</tr>
</tbody>
</table>

SFA: 72% (536) 48% (135) 66% (671)
Popliteal: 15% (114) 17% (48) 16% (162)
Infrapopliteal: 13% (93) 34% (96) 18% (182)

Primary Patency
Claudicant Cohort

PSVR ≤ 3.5 → 82%
PSVR ≤ 2.4 → 78%
Primary Patency by Kaplan-Meier*
Claudicant Cohort

Primary Patency by Lesion Length
Claudicant Cohort (PSVR ≤ 2.4)

Primary Patency by Vessel
Claudicant Cohort (PSVR ≤ 2.4)

DEF LE CLI Cohort Primary Endpoint:
Freedom from Major Amputation at 12 Months

Periprocedural Complications (All Subjects)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Incidence (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal Embolization</td>
<td>3.8% (30)</td>
</tr>
<tr>
<td>No Intervention</td>
<td>2.1% (17)</td>
</tr>
<tr>
<td>Surgical Intervention</td>
<td>0.1% (1)</td>
</tr>
<tr>
<td>Endovascular Intervention</td>
<td>1.5% (12)</td>
</tr>
<tr>
<td>Dissection (flow-limiting)</td>
<td>2.3% (18)</td>
</tr>
<tr>
<td>No Intervention</td>
<td>0.8% (6)</td>
</tr>
<tr>
<td>Surgical Intervention</td>
<td>0.0% (0)</td>
</tr>
<tr>
<td>Endovascular Intervention</td>
<td>1.5% (12)</td>
</tr>
<tr>
<td>Perforation</td>
<td>5.3% (44)</td>
</tr>
<tr>
<td>No Intervention</td>
<td>1.1% (9)</td>
</tr>
<tr>
<td>Surgical Intervention</td>
<td>0.1% (1)</td>
</tr>
<tr>
<td>Endovascular Intervention</td>
<td>4.0% (32)</td>
</tr>
<tr>
<td>OVERALL intervention rate</td>
<td>7.6% (61)</td>
</tr>
</tbody>
</table>

*PSVR ≤ 2.4

Diabetics: 78%
Non-Diabetics: 77%

Diabetes: 78%
Non-Diabetes: 77%

*PSVR < 2.4
A Pilot Study of Antirestenosis Treatment
12-Month Results: Directional Atherectomy Followed by a Paclitaxel-Coated Balloon to Inhibit Restenosis and Maintain Vessel Patency

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Bad Krozingen
Bad Krozingen, Germany

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Key Inclusion and Exclusion Criteria

Inclusion Criteria
1. Rutherford Clinical Category Score of 2, 3 or 4
2. ≥70% stenosis, restenosis or occlusion in the SFA and/or popliteal artery
3. Target lesion(s) length is 7-15 cm
4. Target vessel diameter is ≥4 mm and ≤7 mm

Exclusion Criteria
1. In-stent restenosis
2. Aneurysmal target vessel
3. 2 or more lesions that require treatment in the target limb

Periprocedural Outcomes (per CEC)
Higher Technical Success and Lower Incidence of Flow-Limiting Dissection in DAART RCT Arm

Outcomes | DAART Severe Ca++ Arm | DCB | p-Value (DAART vs. DCB)
--- | --- | --- | ---
Technical Success | 89.6% | 64.2% | 0.004
Distal Embolization | 6% (3/48) | 0% (0/54) | 0.101
No Intervention | 1 0 1
Endovascular Intervention | 2 0 0
Bail-Out Stent | 0% (0/48) | 3.7% (2/54) | 0.50
Dissection (flow-limiting, Grade C/D) | 2% (1/48) | 19% (10/54) | 0.01
No Intervention | 1 6 0
Endovascular Intervention | 0 4 0
Perforation | 4% (2/48) | 0% (0/54) | 0.22
No Intervention | 0 0 0
Endovascular Intervention | 2 0 0

Technical success defined as achieving ≤30% residual stenosis following protocol-defined treatment and before adjunctive therapy (ie post-dilatation). No surgical interventions were required for any patient.

Key Study Outcome at 12 Months
Angiographic Patency

12-Month Patency: DAART RCT Patients
Is it Important to Achieve ≤30% Residual Stenosis with Directional Atherectomy Post-Procedure?

12-Month Results: DAART RCT Patients

EXCITE ISR Trial Overview

DESIGN
Prospective, randomized, multi-center clinical evaluation of excimer laser atherectomy (ELA) for ISR

PRIMARY SAFETY ENDPOINT
Major Adverse Events (MAE) during hospitalization through 37-day follow-up to include all death, unplanned major amputation, or target lesion revascularization

PRIMARY EFFECTIVENESS ENDPOINT
Freedom from clinically driven TLR through 6 month follow-up (212 days)

252 patients enrolled between June 2011 and March 2014 at 40 clinical sites in United States
252 lesions treatable by guidewire
170 ELA + PTA
82 PTA
Primary Safety endpoint at 37 days (n=158)
Primary Safety endpoint at 37 days (n=77)
Primary Safety endpoint at 212 days (n=187)
Primary Safety endpoint at 212 days (n=177)
Baseline Lesion Characteristics

<table>
<thead>
<tr>
<th>ELA + PTA (N=169)</th>
<th>PTA Alone (N=81)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Lesion Length (cm)</td>
<td>19.3</td>
<td>18.9</td>
</tr>
<tr>
<td>Diameter Stenosis (%)</td>
<td>82.0</td>
<td>83.5</td>
</tr>
<tr>
<td>Total Occlusion (%)</td>
<td>21.6</td>
<td>22.5</td>
</tr>
<tr>
<td>TASC C/D (%)</td>
<td>58.9</td>
<td>54.7</td>
</tr>
<tr>
<td>Calcium (Mod/Sev) (%)</td>
<td>27.6</td>
<td>10.0</td>
</tr>
<tr>
<td>SI runoff vessel (%)</td>
<td>38.2</td>
<td>24.4</td>
</tr>
<tr>
<td>Stent Fracture (%)</td>
<td>None</td>
<td>6.0</td>
</tr>
<tr>
<td>Type 1 - 2 (%)</td>
<td>11.0</td>
<td>5.5</td>
</tr>
<tr>
<td>Type 3 and 4 (%)</td>
<td>3.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

- Longest lesions in any IDE peripheral study
- 20% of lesions > 30 cm

Procedural Success

<table>
<thead>
<tr>
<th>ELA+PTA (n=170)</th>
<th>PTA (n=82)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turbo Elite use</td>
<td>79.4</td>
<td>N/A</td>
</tr>
<tr>
<td>Distal protection</td>
<td>40.6</td>
<td>36.5</td>
</tr>
<tr>
<td>Final % Diameter Stenosis (%)</td>
<td>22.0±19.3</td>
<td>25.6±11.8</td>
</tr>
<tr>
<td>Residual Stenosis &gt;30% (%)</td>
<td>4.2</td>
<td>13.4</td>
</tr>
<tr>
<td>Procedural Success*</td>
<td>92.9</td>
<td>81.7</td>
</tr>
</tbody>
</table>

* Achievement of <30% residual stenosis by visual assessment without bailout procedure

Primary Endpoints

- 94.4% Freedom from MAC (30 days) ELA + PTA vs 78.9% PTA
- 78.3% Freedom from TLR (6 months) ELA + PTA vs 52.8% PTA

12 Month Follow Up

<table>
<thead>
<tr>
<th>Laser + PTA</th>
<th>PTA Alone</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with 12 Month Visit*</td>
<td>100 (59%)</td>
<td>42 (51%)</td>
</tr>
<tr>
<td>At FU Average Lesion Length (cm)</td>
<td>19.3</td>
<td>18.9</td>
</tr>
<tr>
<td>At FU TASC C/D Lesion (%)</td>
<td>98.9</td>
<td>96.5</td>
</tr>
<tr>
<td>Withdrawal CPI</td>
<td>241 (4%)</td>
<td>171 (19%)</td>
</tr>
<tr>
<td>Survival (%)</td>
<td>98.3</td>
<td>94.8</td>
</tr>
<tr>
<td>Freedom from TLR (%)</td>
<td>53.8</td>
<td>41.7</td>
</tr>
<tr>
<td>Freedom from Amputation (%)</td>
<td>70.0</td>
<td>75.1</td>
</tr>
<tr>
<td>MAC Average</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>ABI Average</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Rutherford Class Average</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Stent Fracture Grade (%)</td>
<td>2.9**</td>
<td>3.7 (5/170)</td>
</tr>
</tbody>
</table>

* Patients were exited after occurrence of MACE prior to 12 month follow up
** Kaplan-Meier
*** One stent fracture occurred in non-lead stent deployed post treatment
**** Four other minor stent fractures occurred at 1 and 12 M in the ELA+PTA arm. Three minor stent fractures occurred at 12 M in the PTA arm.

TLR Analysis

- Average time to TLR 133 days vs 212 days, PTA alone vs ELA + PTA (p=0.03)
- Previous treatment for ISR and lesion length were independent predictors of TLR
- Overall, ELA + PTA TLR risk reduction 43%
  [HR 0.57, CI 0.38-0.84; p=0.005]
  - 49 % ELA + PTA TLR risk reduction in lesions > 15 cm
    [HR 0.51, CI 0.32-0.81; p=0.004]
  - 53 % ELA + PTA TLR risk reduction in TASC C/D lesions
    [HR 0.47, CI 0.29-0.76; p=0.002]

Conclusions

- Directional atherectomy is safe & effective at 12 months
  - Effective for short, medium and long lesions in claudicants & CLI patients
  - 82% Patency in PTA (6.10cm) in claudicant patients
  - 78% Patency in infra-popliteal (6.0cm) in CLI patients
  - 90% Limb Salvage in CLI patients
- Distal embolization requiring intervention rate of 1.6% independently adjudicated is low and proves safety of SilverHawk for the treatment of infra-inguinal arterial disease. Furthermore, all complication rate needing treatment is 7.6%
- Diabetes perform equally well when treated with directional atherectomy to non-diabetics for claudicants
- Anti Restenosis Therapy may increase patency of complex atherectomy
- Important to obtain <30% residual stenosis with atherectomy
- Excite Trial shows advantage for treatment of ISR over POBA