Directional Atherectomy & Anti-restenotic Therapy (DAART): Hong Kong Experience & Update

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Disclosure

Speaker name:

..............................Bryan Yan...................................................

I have the following potential conflicts of interest to report:

- Consulting: Medtronic, Boston Scientific, Cook Medical, OrbusNeich
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest
Background

• Drug-coated balloons (DCB) have significantly changed the management of femoropopliteal disease

• Randomized controlled trials have demonstrated superior patency rates of DCB over PTA at 2- and 3-years\(^1-3\)

• Beyond RCTs, real world registries with DCB use in more complex disease is associated with increased bail-out stenting (40% to 47%)\(^1,4,5\)

Known Limitations of DCB

- Calcium distribution & severity may affect late lumen loss (LLL) & primary patency
- Calcium may represent a barrier to optimal drug absorption

Is there a need for vessel prep? What does it mean?

- DCB as a ‘stand alone, leave nothing behind’ technology in ‘real world’ patients is questionable
- Vessel prep is improving the local environment prior to leaving something behind (DCB or stent)

Debulking can increase luminal gain prior to DCB use?¹,²
Plaque modification can enhance drug uptake?³,⁴
Plaque modification can reduce flow-limiting dissections?⁵

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Tools for Vessel Preparation

Balloons
- Plain Old Balloon Angioplasty
- Cutting Balloons
- Scoring Balloons
- Controlled-inflation Balloon

Atherectomy Devices
- Directional
- Orbital
- Rotational
- Photoablative
Directional atherectomy + DCB (DAART) combination therapy can overcome main limitations of stand-alone SFA therapies

- DA mechanically recanalize the vessel without overstretch
- DA remove perfusion barrier for better & more homogenous drug uptake
- DA reduce likelihood of bailout stenting & preserve native vessel

<table>
<thead>
<tr>
<th>Unmet Need</th>
<th>PTA</th>
<th>BMS</th>
<th>DES</th>
<th>DCB</th>
<th>DA</th>
<th>DA+DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address recoil, dissections and Ca++</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔+</td>
</tr>
<tr>
<td>Prevent Neointimal Proliferation/Restenosis</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔+</td>
</tr>
<tr>
<td>Minimize permanent implants + preserve future options</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔+</td>
</tr>
</tbody>
</table>
# Existing DAART Data

Few single-center studies & one randomized feasibility study

<table>
<thead>
<tr>
<th>Study (* Core Lab)</th>
<th>Type</th>
<th>Patients</th>
<th>Lesions</th>
<th>Dissection(^5)</th>
<th>BO Stent</th>
<th>30-day MAE</th>
<th>Patency 1-year</th>
<th>Patency &gt;1-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>*DEFINITIVE AR(^1)</td>
<td>DCB(^1)</td>
<td>54</td>
<td>54</td>
<td>19% (10/54)</td>
<td>3.7% (2/54)</td>
<td>NR</td>
<td>89.6%</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>DAART(^1)</td>
<td>48</td>
<td>48</td>
<td>2% (1/48)</td>
<td>0%</td>
<td>0%</td>
<td>93.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DAART-Ca</td>
<td>19</td>
<td>19</td>
<td>0%</td>
<td>5.3% (1/19)</td>
<td></td>
<td>93.4%</td>
<td></td>
</tr>
<tr>
<td>Cioppa(^2)</td>
<td>DAART</td>
<td>30</td>
<td>30</td>
<td>6.7% (2/30)</td>
<td>6.7% (2/30)</td>
<td>13% (4/30) (1-year)</td>
<td>90%</td>
<td>?</td>
</tr>
<tr>
<td>Stavroulakis(^3) (Popliteal)</td>
<td>DAART</td>
<td>21</td>
<td>26</td>
<td>NR</td>
<td>NR</td>
<td>14% (3/21)</td>
<td>95%</td>
<td>90% (18-mo)</td>
</tr>
<tr>
<td>Stavroulakis(^4) (CFA)</td>
<td>DCB</td>
<td>26</td>
<td>26</td>
<td>31% (8/26)</td>
<td>4% (1/26)</td>
<td>NR</td>
<td>68%</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>DAART</td>
<td>21</td>
<td>21</td>
<td>5% (1/21)</td>
<td>5% (1/21)</td>
<td></td>
<td>88%</td>
<td></td>
</tr>
</tbody>
</table>

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5. Zeller, et al., defined dissection as ≥ Grade C while Cioppa, et al., defined dissection via chroma-flow involving more than 60% of cross-sectional diameter with blood flow in the false lumen.
DEFINITIVE AR

Prospective, multicenter, randomized (DAART v DCB); plus non-randomized DAART arm for severely calcified lesions

- 121 subjects (10 sites)
- RCC 2-4; lesion lengths 7-15cm [excluding ISR, aneurysmal target sites and multi-lesion limbs]
- Independent CEC, angiographic & DUS core labs
- Pilot study designed to assess effect of DAART v DCB

DEFINITIVE AR\textsuperscript{1}

DEFINITIVE AR – 1 year

- Patency rates generally favorable
- Lower residual stenosis trended toward higher patency rates

2. MAE (Major Adverse Event) defined as major unplanned amputation of the treated limb, all-cause mortality or clinically-driven target lesion revascularization.
3. Clinically-driven TLR (target lesion revascularization) defined as any reintervention or artery bypass graft surgery involving the target lesion in which the subject has a ≥ 70% diameter stenosis (Peak Systolic Velocity Ratio (PSVR) > 3.5 may substitute if a pre-intervention angiogram is not available) and at least two of the following: worsening RCC, worsening WIQ score, or an ABI drop > 0.15 from baseline.
DEFINITIVE AR: 2-year Extension

Trend towards lower TLR with ≤30% residual stenosis after DA

<table>
<thead>
<tr>
<th>Freedom from TLR: ≤30% residual stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-year Freedom from TLR (%)</td>
</tr>
<tr>
<td>≤30% Residual Stenosis Post-DA</td>
</tr>
<tr>
<td>&gt;30% Residual Stenosis Post-DA</td>
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</tbody>
</table>

FU study to DEFINITIVE AR

- Multicenter, single-arm study
  - Target N ≤ 250
  - ≤ 15 sites in US and Germany
  - RCC 2-4, FPA lesions
  - HawkOne / TurboHawk + IN.PACT Admiral
  - Currently enrolling; target completion estimate 2018

- 4 Questions in need of answers
  - Is the directional atherectomy + DCB paradigm safe in long moderate-severely calcified lesions?
  - How effective is DA in removing calcified atheroma prior to DCB and what can IVUS teach us regarding optimal technique?
  - Does a ≤30% %DS post-DA portend a favorable one year clinical outcome? How is this best assessed?
  - What is the appropriate metric to assess ideal vessel prep (residual %DS by angio or luminal gain, residual plaque burden by IVUS)?
DAART in Hong Kong

• DA & DCB readily available
  – DCB (In.Pac Admiral) 2009
  – Directional atherectomy (SilverHawl/TurboHawk) 2010
  – Directional atherectomy (HawkOne) 2017

• DCB & atherectomy are not reimbursable items
  – Package Deal: DA + DPD + DCB

• Uptake is slow
Case 1: HawkOne

Proximal SFA
Focal
Eccentric
Calcified
In.Pac Admiral 6 x 60mm
Case 2: Re-recurrent DES ISR

DA + DCB
9 months Angio FU
Case 3: Diffuse SFA Disease
Post DAART
Nasty!
Summary

• DCB use in complex & long lesions is associated with increasing provisional stent use (calcium is a potential barrier to DCB effectiveness)

• Vessel preparation with atherectomy can enhance DCB effectiveness by establishing lumen gain & potentially increase drug uptake

• Promise of directional atherectomy + DCB for femoropopliteal lesions is demonstrated in a few studies (one multi-center core lab-adjudicated pilot study)

• Marriage of atherectomy + DCB may bring together the best of two worlds: effective plaque modification / debulking paired with sustained drug presence
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