REALITY: Initial Experience

Ravish Sachar MD FACC
UNC-REX Healthcare
University of North Carolina
Raleigh, NC
I have the following potential conflicts of interest to report:

- ☑ Receipt of grants/research support
  Details: Abbot, Boston Scientific, Gore, Medtronic, Microvention, Surmodics

- ☑ Receipt of honoraria and travel support
  Details: Boston Scientific, Medtronic

- ☐ Employment in industry
  Details:

- ☑ Shareholder in a healthcare company
  Details: Contego Medical

- ☐ Owner of a healthcare company
  Details:

☐ I do not have any potential conflicts of interest to report
History

- 78 Male Patient
- Right LE claudication, Rutherford 3 symptoms
- Hx of Tobacco Use, s/p cessation 3 years ago
- CAD, s/p CABG
- HTN
- Dyslipidemia
Will DCB alone work?

- Diffuse disease mid left SFA - 12 cm
- CTO – approximately 2-3 cm
- Severe Ca++
- 2 V run-off
DCB: Proven superiority over PTA for Fem-pop Disease

In. Pact Pivotal 3 yr. Patency

5 yr. Freedom from TLR
Complex Lesions

- Severe calcification, TASC C/D
- Long Lesions/ Long CTOs
- CFA/popliteal disease
- In-stent restenosis

This is real-world disease!
Lesion Length and Provisional Stenting

Provisional Stent Rates in DCB Trials Trend with Lesion Length

Stent (%) vs Lesion Length (cm)

Can We Achieve Short And Long Term Results With DCB Alone?
DCB Mechanism of Action:
Solid Phase Drug Delivery to Media/Adventitia

PACCOCATH (2009)
Granada JF. Open Heart. 2014

IN.PACT

STELLAREX

Drug Uptake Level

Edelman E. EuroPCR 2015

6 X deeper penetration with OAS
Calcium: Barrier to Drug Penetration?

1. Fanelli F et al Cardiovas Interv Radiol 2014
2. Tepe G. ISET 2014
### Evidence: Published Studies of Atherectomy + DCB

<table>
<thead>
<tr>
<th>Study (* Core Lab)</th>
<th>Type</th>
<th>Patients</th>
<th>Dissection (≥Grade C)</th>
<th>Patency</th>
<th>30-day MAE</th>
<th>1-year</th>
<th>&gt;1-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>*DEFINITIVE AR¹</td>
<td>DA + DCB</td>
<td>48 (DA+DCB) 54 (DCB alone)</td>
<td>2% (1/48) 18.5% (10/54)</td>
<td>BO Stent</td>
<td>2.1% (1/48) NR</td>
<td>84.6%</td>
<td>81.3%</td>
</tr>
<tr>
<td>STAVROULAKIS²</td>
<td>DA+DCB</td>
<td>41 (DA+DCB) 31 (DCB alone)</td>
<td>NR</td>
<td>5% (2/41) 16% (5/31)</td>
<td>NR</td>
<td>85%</td>
<td>65%</td>
</tr>
<tr>
<td>CIOPPA³</td>
<td>DA+DCB</td>
<td>30 (DA + D)</td>
<td>NR</td>
<td>6.5% (2/30)</td>
<td>NR</td>
<td>90%</td>
<td>?</td>
</tr>
<tr>
<td>SIXT⁴</td>
<td>DA+DCB</td>
<td>29 (DA+DCB) 60 (PTA)</td>
<td>NR</td>
<td>12.4%(11/89)</td>
<td>NR</td>
<td>84.7%</td>
<td>43.8%</td>
</tr>
<tr>
<td>GANDINI⁵ ISR</td>
<td>Laser+DCB</td>
<td>24 (Laser+DCB) 24 (DCB alone)</td>
<td>0% 0%</td>
<td>8% (2/24) 0% (0/24)</td>
<td>NR</td>
<td>66.7%</td>
<td>37.5%</td>
</tr>
<tr>
<td>KOKKINIDIS⁶ ISR</td>
<td>Laser+DCB</td>
<td>62 (Laser+DCB) 50(Laser+POBA)</td>
<td>1.6% (1/62) 0% (0/50)</td>
<td>32% 19/60 58% (29/50)</td>
<td>NR</td>
<td>86.7%</td>
<td>56.9%</td>
</tr>
</tbody>
</table>

DEFINITIVE AR Study

2. Defined as dense circumferential calcification extending > 5 cm.
DEFINITIVE AR

1 Yr Angiographic patency

<table>
<thead>
<tr>
<th>Category</th>
<th>ATERECTOMY+DCB</th>
<th>DCB ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>82.4%</td>
<td>71.8%</td>
</tr>
<tr>
<td>Lesions &gt; 10 cm</td>
<td>90.9%</td>
<td>68.8%</td>
</tr>
<tr>
<td>All Severe Ca++</td>
<td>58.3%</td>
<td>42.9%</td>
</tr>
</tbody>
</table>

N=34  N=39  
N=22  N=16  
N=24  N=7
DEFINITIVE AR Study

Increased lumen gain with DA before DCB resulted in improved patency at 12 months.

2. Includes all patients that received DA+DCB in both randomized and non-randomized arms.
Benefits of Atherectomy + DCB

- May provide added benefit in lesions $\geq 10\text{cm}$ & severely calcified lesions

- Good atherectomy ($<30\%$ stenosis after DA alone) may improve patency
The Three Primary Hypotheses of REALITY

1. DA + DCB use in long (8-25 cm lesions) moderate-to-severely calcified lesions is safe and effective, reducing the need for provisional stenting, and promoting 12-mo. primary patency.

2. A <30% post-DA residual %DS is associated with superior 12-mo primary patency

3. The IVUS metric of ‘plaque burden’ post-DA is more sensitive than angiography in predicting 12-mo primary patency
Does the Use of DA Prior to DCB Improve Long-Term Outcomes in Patients With Long Lesions and Calcified Lesions

Co-Principal Investigators

Krishna Rocha-Singh, MD
Chief Scientific Officer
Prairie Heart Institute of Illinois

Brian DeRubertis MD, FACS
Associate Professor of Surgery
UCLA Division of Vascular Surgery

- Medtronic HawkOne™ or TurboHawk™ and IN.PACT™ Admiral™ drug-coated balloon
- Multi-center, international, prospective, single-arm study
- Up to 250 subject at up to 15 sites in EU and US
- Angiographic and duplex ultrasound core lab adjudication – IVUS stopped 6/29/18
- Primary patency is assessed by duplex ultrasound at 12-months
- Patients followed for 24 months for CD-TLR
- Study sponsored and managed by VIVA physicians
- Support from Medtronic through an external research project grant
- Angio, IVUS, and Histology core labs
REALITY: Relevant Inclusion Criteria

- Rutherford Category 2-4
- RVD ≥ 4mm and ≤ 7mm
- ≥70% de novo or restenotic lesion or occlusion in the SFA/popliteal artery,
- Stenosis or occlusion begins 1cm below the profunda-SFA bifurcation; does not extend beyond P2
- Minimum 1 patent infrapopliteal vessel to the foot with ≤ 50% diameter stenosis;
- Grade 3 or 4 intimal, medial and/or mixed calcification per the PACSS as judged by the operator
- Total lesion/occlusion length – up to 6/29/2018
  - ≥ 8 cm and ≤ 18 cm , CTO ≥ 6 cm and ≤10 cm - USA
  - ≥ 8 cm and ≤ 25 cm , CTO ≥ 6 cm and ≤10 cm  EU
- Total lesion/occlusion length – after 6/29/2018:
  - ≥ 8 cm and ≤ 36 cm , CTO ≥ 6 cm and ≤10 cm – USA and EU
REALITY US/EU Clinical Sites
Current enrollment: 91 pts

- Dr. Ravish Sachar – Raleigh, NC
- Dr. Prakash Krishnan – Mt. Sinai, NYC, NY
- Dr. Brian DeRubertis, UCLA
- Dr. Lawrence Garcia, Boston, MA
- Dr. Roger Gammon, Austin, TX
- Dr. Eric Scott, Iowa Methodist, IA
- Dr. Samir Germanwalla, Longview, TX
- Dr. John Winscott, Univ Mississippi, MS
- Dr. Thomas Zeller, Bad Krozingen
- Dr. Giovanni Torsello, Munster
- Dr. Claus Nolte-Ernsting, Mulheim
What Angiographic Metrics Are Adjudicated?

- Calcium Assessment
- Baseline Angiographic Assessment
- Post-DA
- Post-DCB
REALITY: IVUS Sub-Study

Plaque Burden:
An area-based calculation and percentage

Vessel Area: $4\pi r^2$
Lumen Area: $\pi r^2$
Plaque Burden (Area) = $3\pi r^2$

Percent: 75
REALITY: IVUS Plaque Burden Analysis

Baseline IVUS

Post-DA

Post-DCB
REALITY: IVUS Plaque Burden Analysis

Baseline IVUS

Post-DA

Post-DCB

The Lumen Eccentricity Index: The Directional Atherectomy ‘Foot Print’
Histomorphologic Assessment of Extracted Tissue

Histology Core Lab analysis of all tissues extracted

Dysplastic bone formation
Conclusions

Questions REALITY Will Help Answer

• Is the directional atherectomy + DCB paradigm more safe and effective than DCB alone?

• Will the directional atherectomy + DCB paradigm reduce the need for bail our stenting?

• Does a $\leq 30\%$ %DS post-DA portend a favorable one-year clinical outcome?

• What is the appropriate metric to assess ideal vessel prep (residual %DS by angio or luminal gain, residual plaque burden by IVUS)?
REALITY: Initial Experience

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