Interesting Results From The RAPID Trial: RCT Comparing POBA With Legflow® DEBs For Long-Segment SFA Lesions

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On behalf of the RAPID trial collaborators
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Disclosures

• Research grant Cardionovum
• Consultant Medtronic, Endologix Inc
• Advisory Board Member Endologix Inc
• Research Grants BARD, STG, Angiocrine

Rationale DEB

• Antiproliferative:
  - Reduce intimal hyperplasia
  - Inhibit inflammatory response
• Sustained drug-elution is not a necessity to obtain sustained inhibition of restenosis
• No permanent residual material

DCB in SFA; ongoing evidence

22 (presented) Trials, 3 Meta-analysis

7 Proof-of-Concept [1-4-5-6-7]
1 Registry with 2-year functional outcome [8]
3 Explorative studies (DCB, Atherectomy, C-Plus) [9-11]
1 Pivotal RCT DCB vs. PTA [12]
3 Meta-analysis [13-14-15]

DCB in long lesions [16-17-18]
Includes 1 retrospective DCB vs. DES and 1 RCT DCB-BMS vs. BMS

ISR

2013-2014-2015

5 DCB for In-Stent Restenosis [19-20-21-22]
Includes 3 Registries and 1 RCT

2014-2015-2016

2017-2018-2019

TASC C √
TASC D √
ISR

Randomized Trials for Endovascular Treatment of Infragenicular Arterial Disease: Systematic Review and Meta-analysis (Part 1: Above the Knee)

S. Iem, A.P. Conلب, M.S. Bockemühl, T. Blop, T. Blop, B. Boman. Reviewers


Toward a consensus. SFA (Patent) (N = 206)
Exclude duplicates (n = 427)
Full-text assessment for eligibility (n = 40)
Selected for review (n = 39)
Study (N = 39)
Type of trial
Ongoing
Completed
Randomized
Lumped
N = 39
N = 28
N = 1
N = 6
42.9% (17/39)
71.4% (20/28)
28.6% (1/1)
14.3% (6/42)
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EED versus PTA

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DCB in SFA; proof-of-concept

7 Trials / 6 DCB Technologies (6-month LLL Primary Endpoint)

DCB in SFA; short stenoses

7 Trials / 6 DCB Technologies (6-month LLL Primary Endpoint)

Background: DCB and provisional stenting

Scaffolds still needed, likely at rates proportional to lesion complexity

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Provisional stent rates in DCB Trials are a function of lesion length

Background: DCB and provisional stenting

DCB coating pitfalls

- Maintain sufficient drug adherence in dry state
- Drug loss to subsequent folding process
- Uneven coating on balloon surface (undesired peaks)
- Wash off during catheter advancement
- Flaking of drug = risk of PTX contamination

7 Trials / 6 DCB Technologies (6-month LLL Primary Endpoint)

Background: DCB and provisional stenting

Scaffolds still needed, likely at rates proportional to lesion complexity

Legflow® DCB (Cardionovum)

- 0.1 µm invisible small translucent PTX particles
  - Light can't reflex PTX anymore
- Safepax technology
  - Nanocrystalline PTX particles embedded in the drug excipient matrix
  - No thrombembolic risks
  - Excipient: Ammonium Salt Compound

**RAPID trial**

Randomized trial of Legflow® Paclitaxel eluting balloon (LPEB) with stent placement vs. standard PTA with stent placement for the treatment of intermediate (>5 cm and < 15 cm) and long (≥15 cm) lesions of the superficial femoral artery (SFA). The RAPID trial.

Superi interwoven nitinol stent (Abbott)

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**Key inclusions and exclusion criteria**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
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<tbody>
<tr>
<td>Rutherford 2-4</td>
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<tr>
<td>Symptomatic de novo lesions of the SFA</td>
</tr>
<tr>
<td>Length 5-15 cm; &gt;15 cm</td>
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<td>At least one patent below-the-knee artery with uninterrupted flow to the pedal arch</td>
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<table>
<thead>
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<tbody>
<tr>
<td>Contraindication for anticoagulation (Aspirin, Clopidogrel)</td>
</tr>
<tr>
<td>Severe renal failure (e-GFR &lt;30 mL/min/1.73 m²)</td>
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<tr>
<td>Acute, acute on chronic limb ischemia</td>
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**146 / 160 patients included (91%)**

- 72 assigned to CONTROL
  - 71 received CONTROL intervention
    - 6 did not receive CONTROL intervention
- 71 assigned to LPEB
  - 5 patients were LOST TO FOLLOW UP due to withdrawal of consent
  - 6 did not receive LPEB intervention
- All included in analysis
  - 2 patients were excluded due to technical/clinical and procedural failure

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**Baseline patient characteristics**

- Age
- SFA length
Baseline lesion characteristics (89% included patients)

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<thead>
<tr>
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<th>POBA + stent (N=72)</th>
<th>Legflow + stent (N=71)</th>
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<tbody>
<tr>
<td>Intermediate / long-segment (%)</td>
<td>57 vs 45 %</td>
<td>56 vs 44 %</td>
</tr>
<tr>
<td>Median lesion length (cm)</td>
<td>15 (2-26)</td>
<td>15.1 (2-34)</td>
</tr>
<tr>
<td>Occlusion (%)</td>
<td>71.0</td>
<td>69.0</td>
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</table>

Primary patency (24 mths)

- Loss = binary restenosis on duplex (PSVR >2.4)
- Log Rank P=0.2
- Freedom of TLR

Freedom of TLR

Conclusions

- Legflow® DCB first with nanocrystalline PTX particles and stable coating to prevent wash off
- RAPID trial includes challenging "real-world" lesions
  - Long-segment (15 cm) SFA occlusions (70% of patients)
- Preliminary results (91% patients included)
  - Primary patency of RAPID group similar to prosthetic bypass grafts (historical data)
- Freedom of TLR comparable for both groups
- One year data of all RAPID patients in nov 2016

A meta-analysis to compare Dacron versus polytetrafluoroethylene grafts for above-knee femoropopliteal artery bypass

- Primary patency 12 months 66 – 81%
- Primary patency 24 months 52 – 75%
- Dacron superior to PTFE grafts