Ongoing Trials of Drug Delivery Techniques and Improved Stents for BTK Arteries. The Future is Bright

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Potential conflicts of interest

Speaker’s name: Andrej Schmidt
✓ I have the following potential conflicts of interest to report:
Consulting:
Medtronic, Abbott, Boston Scientific, Cook, Cordis, C.R.Bard, Intactvascular, ReFlow Medical, Spectranetics, Upstream Peripheral

Drug-Coated Balloon BTK

Trials which failed to show a benefit / superiority for DCBs BTK
- In.Pact DEEP multicentric, randomized, controlled trial
  ✓ In.Pact Amphilion PTX-eluting balloon vs.
  ✓ Uncoated Amphilion Deep
  Zeller et al. JACC 2014

- Biolux-P-II multicentric, randomized, controlled trial
  ✓ Passeo-18 LUX PTX-eluting balloon vs.
  ✓ Uncoated Passeo-18
  Zeller et al. JACC Intervent 2015

Ongoing: Lutonix BTK Clinical Trial

- 320 patients at 55 global sites,
- Rutherford 4 and 5; randomized 2:1
- Clinical FU and Duplex up to 36 months
- Angiography in a subset of patients at 12 months

- Primary endpoint:
  ✓ Safety at 30 days (Major amputation / major re-intervention)
  ✓ Limb salvage & primary patency at 12 months

Status of Lutonix 014 BTK IDE Study

- 49 Active Sites
- 255 Enrolled Subjects
  - 179 have completed 6 month follow-up
  - 121 have completed 12 month follow-up

- The Safety Data Monitoring Committee has met 7 times (quarterly) and deemed the study safe to continue.

German single center experience with Lutonix® DCB in BTK
presented @ LINC 2015

Sabine Steiner
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Study design

- Retrospective cohort study of patients undergoing BTK interventions using Lutonix® drug coated balloons
- 248 patients treated, 40 lost to follow-up (16%)
- 220 limbs treated in 208 patients
- Clinical follow up:
  - Rate of death
  - BTK re-interventions and target lesion revascularization
  - Minor and major amputations

Interventional Characteristics

<table>
<thead>
<tr>
<th></th>
<th>N=220</th>
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<tbody>
<tr>
<td>No. of devices used, mean± std</td>
<td>2.3 ± 1.1</td>
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<tr>
<td>Cumulative length of devices (mm), mean± std</td>
<td>242 ± 122</td>
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<tr>
<td>Treatment of inflow lesions, %</td>
<td>48</td>
</tr>
<tr>
<td>Femoropopliteal, %</td>
<td>29</td>
</tr>
<tr>
<td>Popliteal, %</td>
<td>19</td>
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<tr>
<td>Rutherford stage before intervention, %</td>
<td></td>
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<tr>
<td>Stage 3</td>
<td>38.7</td>
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<tr>
<td>Stage 4</td>
<td>12.3</td>
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<tr>
<td>Stage 5</td>
<td>46.4</td>
</tr>
<tr>
<td>Stage 6</td>
<td>2.7</td>
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Follow Up Lutonix BTK Registry

- Freedom from TLR
  - At 6 months 89 %
  - At 12 months 77 %
- 9 Major amputations
- All major amputations were performed in CLI patients (6.6% of the CLI cohort)

Different Way of Local Drug-Delivery BTK

The Bullfrog® Micro-Infusion Device
(Mercator MedSystems)

- Revascularization injures the deep layers of the artery
  - Inflammation
  - Progenitor cell differentiation
  - Myofibroblast proliferation
- Injection of dexamethasone / glucose into the deep layers

Bullfrog Adventitial Infusion

<table>
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<tr>
<th>Pre-Revascularization</th>
<th>Post-Revascularization</th>
<th>Post-Infusion</th>
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<td>20% contrast, 80% drug</td>
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Bullfrog Study Program BTK

LIMBO (n=100)
First double blinded RCT BTK
- 50 PTA with Bullfrog vehicle delivery
- 50 PTA with Bullfrog Dexa.- delivery

DANCE (n=300)
- PTA
- Atherectomy
- Bullfrog Dexa.- injection
How to Improve Patency BTK

- What has been proven in randomized trials to lower the restenosis rate in BTK-arteries so far?
  - Drug-eluting stents

Drug-Eluting Bioabsorbable Stents

Everolimus eluting bioresorbable vascular scaffold (Absorb BVS)

Absorb BVS: BTK Pilot-Study

- Single center prospective registry
  - 20 patients, 25 limbs, 23 scaffolds
  - Mean lesion length 20.2 mm
  - Procedural success 100 %

1 year results:
- Clinical improvement 88 %
- Limb salvage 100 %
- Primary patency 94.4 %

Need for longer DES for Diffuse BTK-Disease

- Movement-segment
- Missmach of diameters

Self-expanding long drug-eluting stent preferred

Zilver-PTX 5.0/100 mm
(Not available, not approved for BTK in the US)

Summary

- There is still an unmet need for improved durability in the BTK area.
- Longer DES / drug-eluting scaffold technology might be a solution.
- Drug-delivery via balloon-based solutions may still be the most realistic approach.