Latest data in the field of drug-eluting therapies: What is the current status?

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Disclosure

Speaker name: Sabine Steiner

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest
Restenosis: Begins with Inflammation

Timeframe:
- Hours to Days
- Weeks
- Months

Inhibiting Agents:
- Stenting for Recoil/Dissection; (Dexamethasone injection)
- Drug eluting technologies: Balloons/Stents coated with: Pacitaxel -limus drugs

VESEL INJURY
- Recoil
- Dissection
- Inflammation
- Cell Proliferation, SMC Migration
- ECM Secretion/breakdown
- Fibrosis, Hyperplasia
Drug coated balloons

- **Paclitaxel**
  - Inhibits cell division AND migration

- Single dose exposure to inhibit
  - Long term cellular proliferation
  - Extracellular matrix secretion/breakdown
  - Vascular Smooth Muscle Cell Growth (but not endothelial cells)

- Avoiding a permanently implanted metallic scaffold
Drug coated balloons are different!

Different drug dosages!
Different excipients!
No class effect!

Clinical case: Drug eluting balloons

• Pre-interventional angiogram left leg
Intervention: Left SFA recanalization

DEB angioplasty

Severe dissection after 1. PTA

after prolonged PTA

Final result after spot stenting
Proven efficacy of DCB

- **RCTs**
  - various DCB were superior against standard angioplasty re primary patency and TLR
  - mainly in TASC A/B lesions

- **Registries**
  - good patency rates for DCB in more complex lesions
  - High bail-out stenting rates (≈40% and higher)

- Limited evidence comparing one DCB against another (head-to-head comparisons)
Compare Pilot study (150 patients):
Primary patency through 24 months

For KM-estimates, the study end was harmonized to 770 days for all events censored ≥710 days.

D. Scheinert presented at LINC 2019
Drug eluting stents

- For the SFA 2 drug eluting stents available
  - Zilver PTX: polymer free, paclitaxel-eluting
  - Eluvia: polymer coated, paclitaxel-eluting
Zilver PTX: 5 year results

comparing overall DES (n=318; primary DES + provisional DES) to standard care (n=183; provisional BMS placement + optimal PTA)

Imperial RCT comparing Zilver PTX vs. Eluvia

Primary analysis: Non-inferiority was shown for both efficacy and safety endpoints at 12 months.

Gray WA. et al Lancet. 2018 Oct 27;392:1541-1551
REAL PTX study

Drug-Eluting Stent VS. Drug-Coated Balloon Revascularization in Patients with Femoropopliteal Arterial Disease

JACC 2019; in press
REAL PTX study results – full cohort

Kaplan Meier Estimates of Event-free Survival (EFS), Values Represent Patients

<table>
<thead>
<tr>
<th>Days Post-Procedure</th>
<th>EFS (%) ± Standard Error</th>
<th>Cumulative Failed (n)</th>
<th>Cumulative Censored (n)</th>
<th>Remaining at risk (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DCB</td>
<td>DES</td>
<td>DCB</td>
<td>DES</td>
</tr>
<tr>
<td>0</td>
<td>100±0</td>
<td>100±0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>180</td>
<td>93.1±3.0</td>
<td>94.6±2.6</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>365</td>
<td>79.9±4.8</td>
<td>79.3±5.0</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>730</td>
<td>56.0±6.4</td>
<td>64.6±6.2</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>1095</td>
<td>42.4±6.6</td>
<td>56.7±6.6</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>1155</td>
<td>38.4±6.5</td>
<td>54.5±6.7</td>
<td>37</td>
<td>27</td>
</tr>
</tbody>
</table>

Logrank P=0.17
Difference DCB-DES, 95% CI
1-year: 0.6 [-13.0%, 14.2%]
3-year: -14.3 [-34.4%, 2.2%]
BEST SFA Study: Inclusion of 120 PAD patients Rutherford category 2-4

Femoropopliteal lesions:
Stenoses >10cm, Occlusions >5cm;
Maximum length: ≤30cm

1:1 randomization

Stent-preferred strategy

Stent-avoiding strategy

Vessel preparation for plaque modification/minimizing bail out stenting:
Debulking devices, scoring/high pressure balloons

DES
Supera for focal severe calcification

DCB
Bail-out stenting: BMS, Supera for focal severe calcification

Both strategies feasible at the operator’s discretion
Drug eluting technologies BTK

Challenges of BTK interventions

- Majority performed in CLI patients

- CLI: typically long, occlusive disease and associated with challenging inflow and run-off disease
POBA for CLI Treatment

- 68 CLI patients due to BTK lesions
- Lesion length: 140 ± 90 mm
- Restenosis at 3 months: 73%
- Restenosis delays healing

Short lesions, if full-lesion coverage is possible = DES is standard

Long lesions, full-lesion stenting not reasonable
### Randomized controlled trials of drug-eluting stents in infrapopliteal disease

<table>
<thead>
<tr>
<th>Study/stent type</th>
<th>N</th>
<th>CLI/IC</th>
<th>Control arm</th>
<th>Follow-up, mo</th>
<th>Outcome</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACHILLES</td>
<td>200</td>
<td>CLI + IC</td>
<td>PTA</td>
<td>12</td>
<td>Primary patency</td>
<td>0.025</td>
</tr>
<tr>
<td>Sirolimus-eluting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>75% vs 57%</td>
<td></td>
</tr>
<tr>
<td>DESTINY</td>
<td>140</td>
<td>CLI</td>
<td>BMS</td>
<td>12</td>
<td>Primary patency</td>
<td>&lt;0.001</td>
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<tr>
<td>Everolimus-eluting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>85% vs 54%</td>
<td></td>
</tr>
<tr>
<td>YUKON-BTX</td>
<td>161</td>
<td>CLI + IC</td>
<td>BMS</td>
<td>12</td>
<td>Primary patency</td>
<td>0.004</td>
</tr>
<tr>
<td>Sirolimus-eluting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81% vs 56%</td>
<td></td>
</tr>
<tr>
<td>IDEAS</td>
<td>50</td>
<td>CLI + IC</td>
<td>PCB</td>
<td>6</td>
<td>Restenosis</td>
<td>0.046</td>
</tr>
<tr>
<td>Drug-eluting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28% vs 58%</td>
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</table>

Role of DES BTK

TABLE
Characteristics of 128 Patients With Critical Limb Ischemia Undergoing Tibial Endovascular Revascularization in 139 Limbs

<table>
<thead>
<tr>
<th>Infrapopliteal treatment</th>
<th></th>
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<tbody>
<tr>
<td>Occlusive disease</td>
<td>78 (56.1%)</td>
</tr>
<tr>
<td>Lesion length, mm</td>
<td>78.9±46.1</td>
</tr>
<tr>
<td>TPT (n=23, 16.5%)</td>
<td>32.9±7.8</td>
</tr>
<tr>
<td>ATA (n=58, 41.7%)</td>
<td>76.1±47.0</td>
</tr>
<tr>
<td>PTA (n=37, 26.6%)</td>
<td>81.6±51.2</td>
</tr>
<tr>
<td>PA (n=49, 35.3%)</td>
<td>80.2±41.8</td>
</tr>
<tr>
<td>Drug-eluting balloon</td>
<td>6 (4.3%)</td>
</tr>
<tr>
<td>Stenting</td>
<td>21 (15.1%)</td>
</tr>
<tr>
<td>Drug-eluting stent</td>
<td>7 (5.0%)</td>
</tr>
</tbody>
</table>

“Clinical real-life scenario”

Baumann F et al. J Endovasc Ther 2013,20:149
PTA of Long BTK-Lesions:
Plane Old Balloon is Standard

Occlusion ATA, Stenosis PA  After POBA both arteries  3-Mo Re-Occlusion
## In.Pact Deep study

<table>
<thead>
<tr>
<th></th>
<th>DEB (n=239)</th>
<th>POBA (n=119)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically-driven target lesion revascularisation</td>
<td>11.9%</td>
<td>13.5%</td>
<td>0.68</td>
</tr>
<tr>
<td>Late lumen loss</td>
<td>0.61±0.78mm</td>
<td>0.62±0.78mm</td>
<td>0.95</td>
</tr>
<tr>
<td>Binary restenosis</td>
<td>41%</td>
<td>36%</td>
<td>0.61</td>
</tr>
<tr>
<td>Major Amputation</td>
<td>8.8%</td>
<td>3.6%</td>
<td>0.08</td>
</tr>
</tbody>
</table>

No treatment effect – lack of drug effect?

Zeller et al. J Am Coll Cardiol 2014;64:1568-76
Lutonix BTK study

442 patients randomized in a 2:1 fashion to Lutonix 014 DCB (BD) or PTA
> 90% of patients enrolled had CLI

<table>
<thead>
<tr>
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<th>POBA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy endpoint*</td>
<td>85.3%</td>
<td>70.7%</td>
</tr>
<tr>
<td>Primary safety endpoint**</td>
<td>99.3%</td>
<td>99.4%</td>
</tr>
</tbody>
</table>

*Composite measurement of freedom from target limb occlusion, above ankle amputation, and clinically driven target lesion revascularisation, to define primary patency; KM-estimates; P<0.001

**Freedom from composite all-cause death, above ankle amputation or major reintervention of the treated limb through 30 days

Presented at VIVA; 5–8 November, Las Vegas, USA
Chronic heel ulceration

71-year old patient, diabetic
PTA via the Plantar Arch
PTA via the Plantar Arch

DEB

Standard-balloon
Before treatment

- Slow healing of the ulcer,
- Forefoot clinically unchanged
6 months FU after PTA
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