Drug-coated balloons in BTK: Where do we stand and what are the open questions?

Dr. Marc Bosiers
LINC 2019 - Leipzig
My disclosures

☒ I do not have any potential conflicts of interest to report

☐ 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)
DCB proven to work in SFA

**IN.PACT SFA Trial**

- **1 Year**
  - IN.PACT™ Admiral™ N=220: 87.5%
  - PTA N=111: 55.8%
  - Δ 31.7% p<0.001

- **2 Year**
  - IN.PACT™ Admiral™ N=220: 78.9%
  - PTA N=111: 50.1%
  - Δ 28.8% p<0.001

- **3 Year**
  - IN.PACT™ Admiral™ N=220: 69.5%
  - PTA N=111: 45.1%
  - Δ 24.4% p<0.001
Not all lesions are the same

**ABOVE THE KNEE**
- Mixed morphology (multiple plaque types & thrombus)
  - Medium to large vessels (4-9mm)
  - Rutherford 2-6

**BELOW THE KNEE**
- Lesions more commonly calcified
  - Small vessels (1.5 – 3.5mm)
  - Rutherford 4-6

VIVA 2011 survey – 100 physicians surveyed.
Tibial vessel pathology (Calcium\textsuperscript{+++} and CTO) obstructs drug migration

- Neointimal hyperplasia
- Intimal and medial calcification
- Tickening of the elastic lamina (between intima and media)
Early DCB-BTK evidence showed high promise to reduce restenosis and reintervention rates vs standard PTA.

However, there is no consistency between trials and registries on hard clinical endpoints.

No major differences in hard clinical outcomes across all studies between any DCB and control arm.
No difference in primary patency rates between DCB & PTA at 6MFU in the BIOLUX P-II study.

Also, no difference in amputation rates.

IN.PACT DEEP showed no superior treatment effect of DCB over PTA.

Trend towards a higher amputation rate in the DCB arm.
DCB will be useful in BTK if:

- Safely improves patency rates!
- Reduces the need for TLR!
- Reduction in major amputation rate! (most important endpoint for the treatment of CLI!!!
New studies

BIOLUX P-III (BTK subcohort)

Lutonix BTK Registry

Lutonix RCT

Luminor BTK Registry

IN.Pact BTK
BIOLUX P-III : DCB

• +/- 880 patients
  All comers study in infra-inguinal arteries with BTK cohort (N=150 pts)

• Primary Endpoint:
  Freedom from clinically driven TLR @ 12M

Inclusion criteria:

✓ RCC not specified
✓ Stenosis not specified
✓ LL not specified
**BIOLUX P-III: DCB**

<table>
<thead>
<tr>
<th>Lesion Characteristics</th>
<th>N=184</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length, mm (mean ± SD)</td>
<td>79.0+/−72.0</td>
</tr>
<tr>
<td>Reference Vessel Diameter mm (mean ± SD)</td>
<td>3.0+/−0.6</td>
</tr>
<tr>
<td>Diameter Stenosis (%)</td>
<td>86.3+/−12.7</td>
</tr>
<tr>
<td>Calcification</td>
<td>Heavy</td>
</tr>
<tr>
<td>TASC Classification</td>
<td>59/175 (33.7%)</td>
</tr>
<tr>
<td>A</td>
<td>30/175 (17.1%)</td>
</tr>
<tr>
<td>C</td>
<td>37/175 (21.1%)</td>
</tr>
<tr>
<td>D</td>
<td>49/175 (28.0%)</td>
</tr>
</tbody>
</table>

- 68.9% of lesions calcified
- 49.1% lesions are TASC C/D

76.7% CLI

**BIOLUX P-III BTK subgroup**

| # Subjects | 150 |
| Lesion length (mm +/- SD) | 72.2+/−10.1 |
| CLU | 92/120 (76.7%) |
| | 47/120 (39.2%) |

**Diabetics**

| Freedom from cd TLR* | 92.4% |
| Major target limb amputation* | 7.8% |
| All cause of death* | 9.3% |
| Bailout | 1.1% |

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Prof. Dr. Gunnar Tepe - CX 2018 – BIOLUX P-III : Passeo-18 Lux All-comers Registry: 12 month results in BTK
Global Lutonix DCB BTK Registry - DCB

• +/- 500 patients single arm study - Lutonix DCB

• Primary Endpoint:
  Freedom from clinically driven TLR @ 6M
  Limb Salvage Rate @ 6M

Inclusion criteria:

✓ RCC 3,4,5
✓ Stenosis >70% or occlusion of the BTK arteries
✓ LL not specified
Global Lutonix DCB BTK registry – DCB – prelim results

- MLL : 102 ± 79.5mm
- f-TLR @6M : 89.30%

Dr. M. Lichtenberg – LINC 2018 – Initial Look at the Global Lutonix DCB BTK Registry Study 6M outcomes
Lutonix RCT – DCB vs PTA

• +/- 442 patients RCT - Lutonix DCB vs PTA

• Primary Endpoint:
  Safety: Freedom from Major Adverse Limb Events & all-cause perioperative death

  Efficacy: Limb Salvage and Primary Patency Rate @ 6M

Inclusion criteria:

✓ RCC not specified
✓ Stenosis not specified
✓ LL not specified
### Lutonix RCT – DCB vs PTA

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>DCB</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLI patients</td>
<td>90%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic patients</td>
<td>71.10%</td>
<td>68.40%</td>
<td></td>
</tr>
<tr>
<td>Hypertensive patients</td>
<td>92.00%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia patients</td>
<td>78.40%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>59.20%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Lesion Length</td>
<td>111.80mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcified lesions</td>
<td>59.90%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTO</td>
<td>36.10%</td>
<td>33.30%</td>
<td></td>
</tr>
</tbody>
</table>

**Non-inferiority primary safety endpoint met!**

Free from safety events @ 30 days:
- DCB arm: 99.30%
- PTA arm: 99.40%

Primary efficacy endpoint was met!

Free from primary efficacy events:
- DCB arm: 73.70%
- PTA arm: 63.50%

**No difference in amputation rate**
Luminor Registry : BTK Cohort

• Preliminary 98 patients – 116 lesions

• All comers study in infra-inguinal arteries - BTK cohort

• Primary Endpoint:
Primary Patency Rate @ 12M

Inclusion criteria:

✓ RCC 2,3,4,5
✓ Stenosis >50% or occlusion (of the tibial arteries)
✓ LL 20 to 200mm
Luminor Registry : BTK Subgroup – prelim results

- MLL : 77.90mm
IN.PACT BTK : DCB vs PTA

• Minimum 60 pts – DCB vs PTA

• Chronic Total Occlusion in infrapopliteal arteries - BTK cohort

• Primary Endpoint: Late Lumen Loss @ 9 Months

Inclusion criteria:

✓ RCC 4,5
✓ Occlusion infrapopliteal artery
✓ LL ≥40mm

Awaiting for the first results!
PTA

DCB

LUMINOR BTK REGISTRY
LUTONIX RCT
LUTONIX BTK REGISTRY
BIOLUX P-III
LEIPZIG REGISTRY
DEBATE BTK

BIOLUX P-II

IN.PACT DEEP
Still some open questions....

Is Paclitaxel the right drug? Sirolimus Coated Balloon - Selution

• Use of micro-reservoirs made out of biodegradable polymer intermixed with Sirolimus
  • **Controlled** and **sustained** drug release
  • **Long-term distribution** of Sirolimus into tissue to maintain therapeutic levels

• Novel Cell Adherent Technology – **CAT™**
  • Minimizes **wash-off** during insertion, tracking and lesion crossing
  • Optimizes **drug transfer** to tissue during short-term balloon dilatation
Still some open questions....

The vessel preparation prior to DCB angioplasty might solve the problem of early recoil as one potential failure mode of paclitaxel releasing DCB.

**ADCAT** Prospective, randomized multicentric study:
Atherectomy (Turbohawk, Medtronic) and Paclitaxel-coated balloon angioplasty (Lutonix 14, Bard) for treatment of long atherosclerotic BTK lesions

**OPTIMIZE BTK** multicenter, randomized multicentric study:

*Awaiting for the first results!*
How to improve DCB results in BTK?

• Adequate vessel prep with high pressure, cutting ballon or atherectomy
  - To reduce friction
  - To reduce recoil
  - To potentially improve drug uptake / wall persistence

• Appropriate balloon-to-vessel ratio sizing (to maximize the highest rate of drug transfer)

• Alternative antiproliferative drugs such as “limus” drugs should be explored

• Alternative ways of applying the drug to the adventia (Bullfrog, LIMBO study, dexamethasone)
DCB will be useful in BTK if:

- Safely improves patency rates!
- Reduces the need for TLR!
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Need for RCT!
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