Drug Coated Balloons in BTK disease

Koen Deloose, MD
Below the knee arterial disease

- A heterogeneous, highly diseased vascular bed, small diameters, most of the time severe Ca++ load

- The association between vessel patency and clinical success (wound healing, improved mobility, pain relief) is not well defined

- Level-1 evidence for endovascular therapies limited
The path to the real world...

Proof of Concept
Feasibility Assessing safety and efficacy signals

Pivotal RCT
Level I Gold Standard Ideal conditions Head to head unbiased assessment

Real World Studies
Switching to all comers Allow for extensive subanalysis Ability to detect low rate events

Standard of Care
Technical Clinical Economical endpoints
**Single Center Registry**
- 104 Patients (CLI 82.6%)
- Diabetes 73%
- Mean lesion length 17 cm
- CTO’s 62%

**IN.PACT Amphirion** vs. matched PTA historical cohort

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** Schmidt A et al. Catheter Cardiovasc Interv. 2010 Dec 1;76(7):1047-54
Early DCB-BTK evidence showed high promise for IN.PACT Amphirion to reduce restenosis & reintervention rates vs. standard PTA.
**Single Center RCT**

- 50 Patients (CLI + CI)
- Mean lesion length: 14.8 cm (DCB) vs 12.7 cm (DES); p=0.33

**IN.PACT Amphirion vs DES**

- Binary restenosis: 58% vs. 28% (p=0.045)
- LLL: 1.35 ± 0.2 vs. 1.15 ± 0.3 (p=0.62)
- TLR: 14.3% vs. 7.4% (p=0.21)

>50% Restenosis

Length (cm)

- Group DES: 3.6 ± 1.5
- Group PCB: 4.3 ± 1.6

P=0.16

**First small RCT showed significantly higher restenosis rates of IN.Pact Amphirion vs DES in ±15 cm BTK lesions**
prospective, multi-center 1:1 RCT: DEB vs. POBA

An, although underpowered, RCT with Passeo Lux showed no differences in hard clinical outcomes between DCB and POBA.
IN.PACT Deep showed no "corelab" difference in efficacy between DCB & POBA.

There is a trend towards higher major amputation rates with DCB, although no statistical significant.

There is no evidence of beneficial subgroups.

There are no predictors of failure identified.
IN.PACT Deep showed no “corelab” difference in efficacy between DCB & POBA. There is a trend towards higher major amputation rates with DCB, although no statistical significant. There is no evidence of beneficial subgroups. There are no predictors of failure identified.

- **DEVICE RELATED?**

- **STUDY DESIGN RELATED?**

- **BTK/CLI RELATED?**
### DEVICE RELATED?

<table>
<thead>
<tr>
<th>Coating method</th>
<th>“Old” IN.PACT Amphirion</th>
<th>“New” (Next Gen) IN.PACT Pacific Admiral</th>
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<tbody>
<tr>
<td>Manually-coated on folded balloon</td>
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<td>Automatically-coated on semi-inflated balloon</td>
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<thead>
<tr>
<th>DCB</th>
<th>PTA</th>
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<tr>
<td>0.61±0.78</td>
<td>0.62±0.78</td>
<td>0.950</td>
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**Lack of drug effect?**

Animal studies confirmed balloon material can impact drug delivery:
- New design delivered more drug to vessel → Folds protect the drug
- New design had less residual drug on balloon → Better drug release

With the courtesy of T. Zeller, presented @ LINC 2015
STUDY DESIGN RELATED?

- Too small control arm (2:1 randomization)?
- Too wide eligibility criteria?
- No standardized wound care protocols?
- No standardized major amputation protocols?
- Low angiographic compliance?
- Very favorable major amputation rates in POBA arm?
• Is there an essential physiological difference between SFA and BTK? (IN.PACT SFA vs IN.PACT DEEP)
• Is there an essential difference between CLI and CI patients in PTX response/risk?
CONCLUSION

- No major differences in hard clinical outcomes across all studies between ANY DCB & control group

- **Further research** is mandatory in this DCB-BTK field:
  - Is PTX the best and safest drug in tibial arteries?
  - Is PTX the best and safest drug in CLI patients?
  - Are there more efficient excipients upcoming?
  - What is the best study design for CLI-BTK trials?