Exploring Options to Manage Dissections and Stenting: BIOREACT

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Disclosure

Speaker name: Prof. Patrice B. Mwipatayi

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
Can DCB Alone Fit All?

Provisional stenting rate in DCB trial up to 40%

Stenting indications for DCB femoropopliteal procedures

- Residual stenosis >50% (>30%)
- Flow limiting dissections
- Thrombosis

References:
- BIOLUX P-III all comers: Tepe G, CIRSE 2017
Is DCB+BMS as good as DES?

Combining Passeo-18 Lux And Pulsar Shows

Good 12-month Outcomes In SFA Compared To DES

<table>
<thead>
<tr>
<th></th>
<th>DCB+STENT</th>
<th>DES</th>
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</thead>
<tbody>
<tr>
<td>BIOLUX 4 EVER</td>
<td>89.9</td>
<td>96.4</td>
</tr>
<tr>
<td>DEBAS</td>
<td>93.6</td>
<td>96.4</td>
</tr>
<tr>
<td>ZILVER PTX RCT</td>
<td>82.7</td>
<td>88.5</td>
</tr>
<tr>
<td>ZILVER PTX</td>
<td>90.8</td>
<td>95.4</td>
</tr>
<tr>
<td>Japanese PMS</td>
<td>86.4</td>
<td>79.5</td>
</tr>
<tr>
<td>MAJESTIC ELUVIA</td>
<td>91.0</td>
<td>91.9</td>
</tr>
<tr>
<td>FIM</td>
<td>89.9</td>
<td>88.5</td>
</tr>
<tr>
<td>IMPERIAL RCT</td>
<td>100.0</td>
<td>88.5</td>
</tr>
<tr>
<td>ELUVIA</td>
<td>20.0</td>
<td>95.4</td>
</tr>
<tr>
<td>ZILVER PTX</td>
<td>91.9</td>
<td>91.9</td>
</tr>
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12 mth PP

12 mth fcdTLR

| LL (cm) | 8.3 | 20  | 6.6 | 14.7 | 7.1 | 8.7 | 8.2 |
| PSVR    | 2.5 | 2.5 | 2.0 | 2.4  | 2.5 | 2.4 | 2.4 |

BIOLUX 4 EVER : Deloose K., Presented at CK 2017, 12-month data (365 days)
IMPERIAL RCT : Grey WA. Lancet 2018 (Published online Sept 22, 2018)
DEBAS & BIOLUX 4EVER

Limitations

- Full metal jacket with full lesion stented
- Chronic physical irritation with remodelling
- Long length vessel caging
- Fractures
- Intimal hyperplasia
- In-stent restenosis

LEAVING NOTHING / LESS BEHIND?

Slide courtesy from Dr. K. Deloose

BIOLUX 4 EVER: Deloose K., Presented at CX 2017, 12-month data (365 days)

IMPERIAL RCT: Gray WA. Lancet 2018 (Published online Sept 22, 2018)
How REACT approach differs?

POBA
Predilation at least 3’
Slow inflation

Passeo-18 Lux

Pulsar-18 (BMS)
*As Less as Reasonably Achievable (ALARA)*
+ post dilation at the physician discretion

Satisfactory

Mission accomplished

Unsatisfactory

Mission accomplished
How REACT refines Stenting?

- Consensus on stent requirement to treat elastic recoil and flow limiting dissection
- No clear definition for flow limiting dissection in peripheral artery
- Should a dissection be treated or observed?
- Full lesion stenting or spot stenting?
- How to improve procedural hemodynamic assessment and related stenting approach?
BIO REACT Pilot Study Design

<table>
<thead>
<tr>
<th>Design</th>
<th>Global Multicenter <strong>Prospective, Pilot Diagnostic Study</strong></th>
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</table>
| Objectives | □ Evaluate the utility of adjunctive procedural assessments to identify post drug-coated balloon flow limiting dissection and/or stenosis additional to conventional angiography  
  ▪ Intra-operative Duplex Ultrasound (Core lab controlled)  
  ▪ Intra-arterial pressure measurement (IAP)+ IVUS (Core lab controlled)  
  □ Estimate REACT algorithm clinical performance  
  □ Health care resources assessment |
## Participating Centers

<table>
<thead>
<tr>
<th>Country</th>
<th>Sites</th>
</tr>
</thead>
</table>
| Belgium | ▪ A.Z. Sint-Blasius, Dendermonde (Dr K. Deloose)  
▪ Onze-Lieve-Vrouwziekenhuis, Aalst (Dr L. Maene)  
▪ ZOL Genk (Dr W. Lansink) |
| France  | ▪ University Hospital of Nantes (Pr Y. Gouëffic) |
| Austria | ▪ Medical University, Graz (Pr M. Brodmann)  
▪ Medical University Vienna (Pr C. Loewe) |
| Germany | ▪ Arnsberg Clinic, Arnsberg (Dr M. Lichtenberg)  
▪ Universität Herzzentrum, Freiburg-Bad Krozingen (Pr T. Zeller)  
▪ University Hospital Leipzig Heart Center, Leipzig (Pr D. Scheinert) |
| Australia | ▪ Royal Perth Hospital, Perth (Pr P.B. Mwipatayi) |
| Spain   | ▪ University Hospital, Guadalajara (Dra M. Guerra) |

- FPI: September 2018
- 10 subjects enrolled
### Primary Endpoints
The primary objective of the study is to evaluate the diagnostic performance of **intra-procedural DUS (core lab controlled)** added to angiography compared to angiography alone:
- Specificity and sensitivity will be calculated for various peak systolic velocity ratio (PSVR) values
- Determination of optimal cut-off via ROC curve

### Secondary Endpoints (selected)
- Diagnostic performance of IAP + IVUS
- Stenting rate, Nb of stents/lesion, stented length (full, spot)
- Primary Patency, cd-TLR, MAE
- Health care costs
### Inclusion / Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>De novo, restenotic or (re)occluded lesion(s) post PTA in the native superficial femoral artery and or the proximal popliteal arteries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>▪ RC 2-4</td>
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<td></td>
<td>▪ RVD ≥ 4 and ≤ 7 mm</td>
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<thead>
<tr>
<th>Exclusion Criteria</th>
<th>ISR</th>
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<tr>
<td></td>
<td>▪ Use of atherectomy, laser or other debulking devices during the index procedure</td>
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</table>

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<thead>
<tr>
<th>Subgroups</th>
<th>Outcomes will be analyzed by different pre-defined subgroups, such as lesion length &lt;15 cm vs &gt;=15 cm; TASC A/B vs C/D; CLI vs non CLI, to investigate the consistency of results.</th>
</tr>
</thead>
</table>

| Sample size        | 150 subjects                                                                                                                         |

| Study duration     | Enrolment : 12 months / FUP : 1, 6 and 12 months                                                                                     |
**PROCEDURAL FLOW CHART**

1. **Predilation**
   - **Passeo-18**

2. **Passeo-18 Lux**

3. **2 planes angiography**

4. **DUS**
   - *(or IAP + IVUS)*

**Final treatment with or without stent based on angiography and adjunctive evaluation findings**

* IAP+/-IVUS will be conducted exclusively at pre-specified trained centers

**Independent Review Committee:**
- Dissection grade (A-F),
- Type of dissection FLD or not FLD
- Whether a stent is needed: Full or Spot stenting

**Passeo-18 balloon Platform**
- Paclitaxel: 3 μg/mm²
- Excipient: BTHC
- Safe guard insertion aid

**Pulsar-18**
- Where needed
Diagnostic Performance

Adjunctive DUS + Angiography vs Angiography alone

- **Sensitivity**: rate of true positive, based on the subjects with a clear FLD diagnosed by angiography = \( \frac{TP}{TP + FN} \)

- **Specificity**: rate of true negative, based on the subjects with no FLD diagnosed by angiography = \( \frac{TN}{FP + TN} \)

<table>
<thead>
<tr>
<th>Angio+adjunctive DUS (1)</th>
<th>Angiography (independent Committee)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FLD (+)</td>
</tr>
<tr>
<td>FLD (+)</td>
<td>True positive (TP)</td>
</tr>
<tr>
<td>FLD (-)</td>
<td>False negative (FN)</td>
</tr>
</tbody>
</table>

IAP+/IVUS will be conducted exclusively at pre-specified trained centers
BIOREACT Case

48 years old patient diabetic with heel ulcer
BIOREACT Case
BIOREACT Case
Independent Review Committee:
- Dissection grade (A-F)?
- FLD or not FLD?
- stent needed?
- full, spot stenting?
BIOREACT Case
CONCLUSIONS

- DCB alone for complex lesions doesn’t work:
  “leaving nothing behind is a dream”
- Combination DCB + BMS seems to work good and can be benchmarked with DES
- Defining – evaluating – deciding on recoil & flow limiting dissections on angiography alone is extremely difficult and subjective
- BIO REACT pilot study evaluates the extra value of intra-operative DUS, IAP & IVUS to angiography alone, following the REACT strategy
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