The utility of transcutaneous ultrasound to determine procedural endpoints – the BIO REACT study concept

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Disclosure slide

Speaker name: Koen Deloose, MD

- I have the following potential conflicts of interest to report:
  - Consulting: Abbott, BD, Biotronik, Boston Scientific, Cook, CTI vascular, iVascular, Medtronic, Philips, Terumo, CyndRX, Profusa
  - Employment in industry
  - Stockholder of a healthcare company
  - Owner of a healthcare company
  - Other(s)

- I do not have any potential conflict of interest
Recommendations

While further investigation is in progress, the FAMHP takes this safety signal very seriously and makes the following recommendations (FR - NL) to healthcare professionals:

- **Do not use paclitaxel DCBs or DESs as a preferred treatment for intermittent claudication until further notice.** Carefully estimate the risks and benefits for each patient.
- **Discuss the risks and benefits of all available treatment options for PAV** with patients. Inform patients about the uncertainty of increased mortality.
- **Ensure proper follow-up** for patients who have already been treated with a paclitaxel DCB or DES.
- **Report any adverse event** involving a paclitaxel DCB or DES to FAMHP using our online adverse event form.

Patients who are worried or have any questions about these aids should talk to their attending physician.

**Federal Agency for Medicines and Health Product, July 3rd 2019**
How to continue...?

Heavily calcified

High Risk Restenosis

Vessel Prepping Responder
“3 questions/answers”-based treatment algorithm

Severe Calcium

Angioplasty Responder

- **Focal non-responding Ca**
  - **SUPERA**
- **Diffuse non-responding Ca**
  - **ATHERECTOMY + SUPERA**
  - **PAVE & CRACK BYPASS**

High Risk Restenosis

- **Angioplasty responder**
  - **DCB**
  - **DES**
  - **BMS with correct COF**
“3 questions/answers”- based treatment algorithm

- Angioplasty Responder
  - Y: Severe Calcium
    - Y: TO SCAFFOLD OR NOT TO SCAFFOLD...THAT ‘S THE QUESTION
    - N: Focal non-responding Ca
      - Y: SUPERA
      - N: Atherectomy + SUPERA
    - N: Diffuse non-responding Ca
      - Y: PAVE & CRACK
      - N: DCB
      - N: DES
      - N: BMS with correct COF
  - N: TO SCAFFOLD OR NOT TO SCAFFOLD...THAT ‘S THE QUESTION
    - N: Angioplasty responder
We need to scaffold a lot...

Provisional stenting rate in DCB trial up to 40% in real-world studies

- Full lesion stenting: full metal jacket
- Chronic physical irritation
- Long length vessel caging
- Fractures
- Intimal Hyperplasia
- In-stent restenosis

LEAVING NOTHING/LESS BEHIND (ALARAS)
We need to scaffold a lot...but...

- No 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?
- How to improve procedural hemodynamic assessment and related stenting approach?
### Design

#### Global Multicenter Prospective Pilot Diagnostic Study

<table>
<thead>
<tr>
<th>Objective</th>
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<tbody>
<tr>
<td>• Evaluation of adjunctive procedural assessments to diagnose post drug-coated balloon flow-limiting dissection/residual stenosis additional to angiography</td>
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<tr>
<td>* intra-operative DUS (core lab controlled)</td>
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<td>* intra-arterial pressure gradient measurement (IAP) +/- IVUS</td>
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<td>• Estimation Biotroniks’ REACT algorithm clinical performance</td>
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<td>• Assessment health care resources</td>
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## BIO REACT PILOT STUDY

<table>
<thead>
<tr>
<th>Country</th>
<th>Sites</th>
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<tbody>
<tr>
<td>Belgium</td>
<td>▪ A.Z. Sint-Blasius, Dendermonde (Dr K. Deloose)</td>
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<td>▪ Onze-Lieve-Vrouwziekenhuis, Aalst (Dr L. Maene)</td>
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<td>▪ ZOL Genk (Dr W. Lansink)</td>
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<td>▪ Groeninghe Kortrijk (Dr P. Lerut)</td>
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<td>France</td>
<td>▪ University Hospital of Nantes (Pr Y. Gouëffic)</td>
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<td>Austria</td>
<td>▪ Medical University, Graz (Pr M. Brodmann)</td>
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<td>▪ Medical University Vienna (Pr C. Loewe)</td>
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<td>Germany</td>
<td>▪ Arnsberg Clinic, Arnsberg (Dr M. Lichtenberg)</td>
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<td>▪ Universität Herzzentrum, Freiburg-Bad Krozingen (Pr T. Zeller)</td>
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<td>▪ University Hospital Leipzig Heart Center, Leipzig (Pr D. Scheinert)</td>
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<tr>
<td>Australia</td>
<td>▪ Royal Perth Hospital, Perth (Pr P.B. Mwipatayi)</td>
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<tr>
<td>Spain</td>
<td>▪ University Hospital, Guadalajara (Dra M. Guerra)</td>
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- FPI: September 2018
- 76/150 subjects enrolled
### BIO REACT PILOT STUDY

#### Primary Endpoints

Evaluate the diagnostic performance of (core lab controlled) *intra-procedural DUS* added to angiography compared to angiography alone:

- Specificity/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, cdTLR, MAE
- Health care costs
### Inclusion Criteria
- De novo, restenotic or (re)occluded lesion(s) post PTA in the native superficial femoral artery and or the proximal popliteal arteries
- RC 2-4
- RVD ≥ 4 and ≤ 7 mm

### Exclusion Criteria
- ISR
- Use of debulking devices during the index procedure

### Subgroups
Outcomes will be analyzed by different pre-defined subgroups:
- lesion length <15 cm vs ≥15 cm; TASC A/B vs C/D; CLI vs non CLI

### Sample size
- 150 subjects

### Study duration
- FUP: 1, 6 and 12 months
PASSEO LUX BALLOON

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

BIOTRONIK

PULSAR 18 STENT

Catheter type, GW
OTW, 0.018”

Struts dimensions
Thickness : 140 μm ; Width : 85 μm

Stent coating
proBIO (Amorphous Silicon Carbide)

Stent markers
6 gold markers at each end

Proximal Shaft
3.6F, hydrophobic coated

IN/EXCLUSION CRITERIA
RESPONDING LESION/PATIENT

INTRALUMINAL/SUBINTIMAL GW PASSAGE
BIO REACT PILOT STUDY

**OPERATOR**

1. PREDILATATION PASSEO 18
2. DILATATION PASSEO 18 LUX
3. 2 PLANES ANGIOGRAPHY
4. INTRA OPERATIVE DUS (or IAP + IVUS*)

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

Final treatment with/without stent based on angiography & adjunctive evaluation findings

**Independent Review Committee**
- Dissection grade (A-F)?
- FLD or not FLD?
- stent needed?
- full, spot stenting?

**NO PULSAR 18 STENT**
BIO REACT PILOT STUDY

Evaluation of the diagnostic performance:

**Adjunctive DUS + Angiography** vs **Angiography alone**

* (operator) vs (independent Committee)

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

<table>
<thead>
<tr>
<th>Angio+adjunctive DUS*</th>
<th>FLD (+)</th>
<th>FLD (-)</th>
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<tr>
<td>FLD (+)</td>
<td>True positive (TP)</td>
<td>False positive (FP)</td>
</tr>
<tr>
<td>FLD (-)</td>
<td>False negative (FN)</td>
<td>True negative (TN)</td>
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* IAP+/-IVUS will be conducted exclusively at pre-specified trained centers
• **History**
  2015 CABG
  2017 PTAS left SFA
  2017 symptomatic CAS right

• **Risk factors**
  Hypercholesterolemia
  Arterial hypertension
  BMI 34

• **Present state**
  Invalidating claudicatio right leg
  (perimeter 120 m) – Rutherford 3

• **Clinical information**
  Good right CFA pulses, no popliteal nor distal pulses
  DUS shows an occlusion of the right mid-SFA with reinjection in distal SFA
BIO REACT PILOT STUDY

: a Case

- Passeo 18 5-200
- Passeo 18 LUX 6-120 (3x)
BIO REACT PILOT STUDY: a Case

**OPERATOR**

- **PREDILATATION PASSEO 18**
- **DILATATION PASSEO 18 LUX**
- **2 PLANES ANGIOGRAPHY**
- **INTRA OPERATIVE DUS (or IAP + IVUS*)**

**Independent Review Committee**
- Dissection grade (A-F)?
- FLD or not FLD?
- Stent needed?
- Full, spot stenting?

**Final treatment with/without stent based on angiography & adjunctive evaluation findings**

**Intra-operative DUS by operator**
BIO REACT PILOT STUDY: a Case

Stenting middle portion SFA
BIO REACT PILOT STUDY: a Case

- **OPERATOR**
  - Predilatation PASSEO 18
  - Dilatation PASSEO 18 LUX
  - 2 Planes Angiography
    - INTRA OPERATIVE DUS (or IAP + IVUS*)

  - Pulsar 18 Stent
    - Spot? Length?...

  - Final treatment with/without stent based on angiography & adjunctive evaluation findings

- **Independent Review Committee**
  - Dissection grade (A-F)?
  - FLD or not FLD?
  - Stent needed?
  - Full, spot stenting?

- **Pulsar 18 Stent 6-120**

  - NO PULSAR 18 STENT
BIO REACT PILOT STUDY: a Case

Final result:
- 5 cm post bif
- 14 cm post bif
- 24 cm post bif

Operator:
- Predilatation Passeo 18
- Dilatation Passeo 18 Lux
- 2 Planes Angiography
- Intraoperative DUS (or IAP + IVUS*)

Final treatment with/without stent based on angiography & adjunctive evaluation findings.

Pulsar 18 Stent Spot? Length?...
BIO REACT PILOT STUDY

Evaluation of the diagnostic performance:

Adjunctive DUS + Angiography (operator) vs Angiography alone (independent Committee)

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**Sensitivity**: rate of true positive, based on subjects with clear FLD diagnosed by angiography = TP / (TP + FN)
Summary

• DCB in combination with stenting seems today one of the key treatments for fempop disease, definitely in patients at high risk for restenosis and reinterventions

• The As Less As Reasonably Achievable Stenting seems to avoid metallic overload complications

• 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 compared to angiography alone: (preliminary) results are expected very soon
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