12 months data from the EffPac randomized clinical trial

Marcus Thieme, MD
REGIOMED Vascular Center and Jena University Hospital

on behalf of the investigators

Disclosure of conflict of interest

• Speaker name: Marcus Thieme, MD

• Potential conflicts of interest related to the presentation:
  o Research support, honorarium: iVascular
Multicenter Randomized Controlled Trial to Assess the Effectiveness of Paclitaxel-coated Luminor® Balloon Catheter vs. Uncoated Balloon Catheter in the Superficial Femoral and Popliteal Arteries to Prevent Vessel Restenosis or Reocclusion
Proprietary nanotechnology dosage system for an uniform, flexible and ultrathin coating

**Excipient** 20%
- Organic ester
- Biocompatible
- Lipophilic

**Paclitaxel** 80%
- Lipophilic
- Inhibition of stenosis
- Specific cellular receptors

- Ultrasound
  - Spray Technology
  - Dosage of uniform diameter nanodrops by ultrasonic deposition

- Uniform coating
  - Homogeneous drug dose

**Multi-layer technology**
- Coating durability during the procedure
- No cracking

**Dry-off**
- Microcrystalline structure
- Optimal drug transfer to the vessel wall within 30-60s seconds
Dosage of uniform diameter nanodrops by direct ultrasonic deposition

- Ultrathin multilayer coating:
  - Increases adhesion to balloon
  - Lower loss related to manipulation
  - Improves durability
  - Lower loss during navigation
  - Improves mechanical properties
  - Fast absorption: 30-60s
EffPac-Trial

**Design:**
Investigator-initiated, prospective, multi-centre, intention-to-treat trial and 2 arms-randomized study

**Objective:**
Safety and efficacy of the Luminor® Paclitaxel drug-eluting balloon in inhibiting restenosis and in ensuring long-term patency

**Sponsor:** University of Jena, Germany

**Representative of the sponsor:** Prof. Dr. Ulf Teichgräber, Jena University Hospital
11 Participating Sites

01 Jena  
PD Dr. R. Aschenbach, *University Hospital Jena*

02 Leipzig  
Prof. Dr. Dierk Scheinert, *University Hospital Leipzig*

03 Bad Krozingen  
Prof. Dr. Thomas Zeller, *Heart Center*

04 Hamburg  
Dr. S. Sixt, Dr. S. Brucks, *Angiologikum*

05 München  
PD Dr. M. Treitl, *University Hospital*

06 Berlin  
Prof. Dr. K. Brechtel, „*Ihre Radiologen*“

07 Sonneberg  
Dr. M. Thieme, *Medinos Clinic*

08 Karlsbad  
Prof. Dr. E. Blessing, *SRH-Clinic*

09 Heidelberg  
Dr. B. Vogel, Dr. C. Erbel, University Heidelberg

10 Arnsberg  
Dr. M. Lichtenberg, *Clinic Arnsberg*

11 Kusel  
Dr. P. von Flotow, *Westpfalz Clinic*
Flowchart

Intraluminal guidewire passage

1. Angiography

Pre-dilatation with POBA

2. Angiography

RANDOMIZATION

POBA

LUMINOR-35® DEB

Inflation time 60±10 sec (both study arms)

3. Angiography

Unsuccessful or subintimal guidewire passage

Exclusion

Non-flow-limiting or flow-limiting dissection

Prolonged PTA with same PTA balloon (Inflation time 120 sec)

Inclusion

Persisting flow-limiting dissection

Bailout Stenting

Inclusion
# Trial Design and Endpoints

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Baseline</th>
<th>6 month</th>
<th>12 month</th>
<th>24 month</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td>Vessel diameter (mm)</td>
<td>• Late Lumen Loss (LLL)</td>
<td>-</td>
<td>-</td>
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<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
<td>• Freedom from Target Lesion Revascularization (TLR/TVR)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Patency*</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Change of ABI, Rutherford stage, QoL (WIQ), EQ-5D</td>
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<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>Primary</td>
<td>• Major and minor amputation rate at index limb</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Mortality, independently of cause</td>
<td></td>
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</tbody>
</table>
171/172 subjects enrolled

Randomization (1:1)

POBA  N= 86

Analyzable*: N=76
Primary Endpoint: N=60

Luminor35  N= 85

Analyzable*: N=76
Primary Endpoint: N=53

Analyzable*: N=76


6 month follow-up

Data Lock: 31.08.2017

12 month follow-up

Data Lock: 31.01.2018

* Patients with data of at least one endpoint
Efficacy: Late Lumen Loss - LLL

* LLL = difference between the diameters (in mm) post-procedure minus 6 months follow-up

<table>
<thead>
<tr>
<th></th>
<th>LUMINOR®</th>
<th>POBA</th>
<th>Difference, 95% CI (LUMINOR® vs. POBA)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLL 6M (mm)*</td>
<td>0.14 [CI: -0.38; 0.67]</td>
<td>1.06 [CI: 0.54; 1.59]</td>
<td>-0.92 [CI: -1.36; -0.49]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Estimated LLL (Mean, 95% CI) from linear mixed model adjusted for center
### Efficacy: Late Lumen Loss - LLL

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug-coated balloon 6 mo LLL (mm)</th>
<th>Control 6 mo LLL (mm)</th>
<th>LLL Difference (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>THUNDER Tepe et al. 2008</td>
<td>0.4±1.2</td>
<td>1.7±1.8</td>
<td>-1.3</td>
</tr>
<tr>
<td>Paccocath coating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AcoArt I Trial Jia et al. 2016</td>
<td>0.05±0.73</td>
<td>1.15±0.89</td>
<td>-1.1</td>
</tr>
<tr>
<td>Orchid (Acotec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFFPAC 2017 Luminor (iVascular)</td>
<td>0.14 [CI: -0.38; 0.67]</td>
<td>1.06 [CI:0.54; 1.59]</td>
<td>-0.92</td>
</tr>
<tr>
<td>RANGER Bausback et al. 2017</td>
<td>-0.16±0.99</td>
<td>0.76±1.4</td>
<td>-0.92</td>
</tr>
<tr>
<td>Ranger DCB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LEVANT I Scheinert et al. 2014</td>
<td>0.46±1.13</td>
<td>1.09±1.07</td>
<td>-0.63</td>
</tr>
<tr>
<td>Lutonix (Bard)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIOLUX P-I Trial Scheinert et al. 2015</td>
<td>0.51±0.72</td>
<td>1.04±1.0</td>
<td>-0.53</td>
</tr>
<tr>
<td>Passeo-18 Lux (Biotronik)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEMPAC Werk et al. 2008</td>
<td>0.5±1.1</td>
<td>1.0±1.1</td>
<td>-0.5</td>
</tr>
<tr>
<td>Paccocath DCB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONSEQUENT 2017 SeQuent Please (B. Braun)</td>
<td>0.35 [CI: 0.19; 0.79]</td>
<td>0.72 [CI: 0.68; 1.22]</td>
<td>-0.37</td>
</tr>
</tbody>
</table>
# Efficacy: Target Lesion Revascularization (TLR)

<table>
<thead>
<tr>
<th></th>
<th>LUMINOR®</th>
<th>POBA</th>
<th>Relative Risk, 95% CI (LUMINOR® vs. POBA)</th>
<th>Number needed to treat (NNT)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR 12M (%)</td>
<td>1.3 (1/76)</td>
<td>18.7 (14/75)</td>
<td>0.08 [0.01; 0.53]*</td>
<td>6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Relative Risk Reduction (RRR) = 91.8%, Cochran-Mantel-Haenszel estimate, adjusted for center
Efficacy: Target Lesion Revascularization (TLR)

POBA

Luminor®

Follow-up (Days)

Patients with Freedom from TLR

+ Censored
## Efficacy: Patency

<table>
<thead>
<tr>
<th></th>
<th>LUMINOR®</th>
<th>POBA</th>
<th>Relative Risk*, 95% CI (LUMINOR® vs. POBA)</th>
<th>Number needed to treat (NNT)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patency (%)</td>
<td>90.3 (65/72)</td>
<td>65.3 (47/72)</td>
<td>1.38 [1.14; 1.67]</td>
<td>4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Interpretation: Relative chance for patency is increased by 38% in the LUMINOR® group

**Primary patency:** Freedom from restenosis (determined by duplex ultrasound PSVR <2.5) and freedom from TLR at 12 months
### Efficacy: Improvement of Rutherford DEB vs POBA *

<table>
<thead>
<tr>
<th>Improvement of Rutherford Stages*</th>
<th>LUMINOR®</th>
<th>POBA</th>
<th>LUMINOR®</th>
<th>POBA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6M</td>
<td>12M**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deterioration of 1 stage</td>
<td>1.4% (1/74)</td>
<td>0% (0/72)</td>
<td>1.3% (1/75)</td>
<td>2.8% (2/72)</td>
</tr>
<tr>
<td>No improvement</td>
<td>13.5% (10/74)</td>
<td>25.0% (18/72)</td>
<td>8.0% (6/75)</td>
<td>20.8% (15/72)</td>
</tr>
<tr>
<td>Improvement of 1 stage</td>
<td>12.2% (9/74)</td>
<td>20.8% (15/72)</td>
<td>17.3% (13/75)</td>
<td>19.4% (14/72)</td>
</tr>
<tr>
<td>Improvement of 2 stages</td>
<td>28.4% (21/74)</td>
<td>26.4% (19/72)</td>
<td>24.0% (18/75)</td>
<td>27.8% (20/72)</td>
</tr>
<tr>
<td>Improvement of 3 stages</td>
<td>44.6% (33/74)</td>
<td>27.8% (20/72)</td>
<td>49.3% (37/75)</td>
<td>29.2% (21/72)</td>
</tr>
</tbody>
</table>

* In comparison to baseline
** In case of TLR, 6M results were used
*** Cochran-Mantel-Haenszel method,
**** Mann-Whitney U test

\[
p = 0.021^{***}/\quad p = 0.015^{****}
\]

\[
p = 0.055^{***}/\quad p = 0.006^{****}
\]
Safety: Mortality after 12 months

<table>
<thead>
<tr>
<th></th>
<th>LUMINOR®</th>
<th>POBA</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (%)</td>
<td>1.2 (1*/85)</td>
<td>2.3 (2*/86)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

* Not related to device or procedure
Conclusions

The LUMINOR® Paclitaxel-coated balloon catheter demonstrates to be clinical highly effective and safe in inhibiting restenosis compared to POBA.

The innovative coating technique matters and is shown not only in the patency, LLL and TLR data, but also in an improvement of the Rutherford stage.

The results of the study allow direct comparison to other already-completed RCTs applying Paclitaxel-coated DEB from different manufacturers in the same target vessel.
Thank you for your attention!

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on behalf of the investigators