EffPac-Trial: Effectiveness of Luminor® DCB vs. POBA in the SFA: primary endpoint and 12-months results

Ulf Teichgräber, MD, MBA
on behalf of the investigators


Disclosure of conflict of interest

• Speaker name: Ulf Teichgräber, MD, MBA

• Potential conflicts of interest related to the presentation:
  o Research grant: iVascular, Endoscout

• Potential conflicts of interest not related to the presentation:
  o Master research agreements with Siemens Healthineers, GE Healthcare
luminor
Paclitaxel coated balloon
(3.0 µg/mm²)

Ultra low tip and crossing profiles

Fast deflation

Complete balloon range dimensions
Luminor 35: 5-7mm Ø and 20-150mm length
Luminor 18: 2-8 mm Ø and 20-200mm length
Luminor 14: 1.5-4mm Ø and 40-200mm length

Innovative and UNIQUE nanotechnology coating

Proprietary nanotechnology dosage system for an **uniform**, **flexible** and **ultrathin coating**

**luminor**

**UNIQUE nanotechnology coating**

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

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

**Spray Technology**
Dosage of uniform diameter nanodrops by ultrasonic deposition

**Ultrasound**

**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

Coating Technology

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

Dosage of uniform diameter nanodrops by direct ultrasonic deposition
Study Title

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
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
EffPac-Trial

**CoreLab:** Dr. Ulrich Beschorner, coreLab Bad Krozingen GmbH, Germany

**Data Safety and Monitoring Board (DSMB):**
Dr. Michael Werk, Martin Luther Krankenhaus, Berlin, Germany
Dr. Vicenc Riambau, Hospital Clinic de Barcelona, Spain
Prof. Dr. Wienke, University Halle-Wittenberg, Germany

**Monitoring (VascuScience GmbH):** Dr. Christin Ott, Svenja Peters, Leipzig, Germany

**Project Management:** Nicole Brillinger, Tabitha Heller, University Hospital Jena, Germany

**SAE Management:** Monique Philipp, University Hospital Jena, Germany

**Data Management:** Cornelia Eichhorn, University Hospital Jena, Germany

**Producer of the Investigational Product:** Life Vascular Devices Biotech, S.L., Barcelona, Spain
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>Efficacy</strong></td>
<td>Vessel diameter (mm)</td>
<td>• Late Lumen Loss (LLL)</td>
<td>• Freedom from Target Lesion Revascularization (TLR/TVR)</td>
<td>• Patency*</td>
</tr>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>Primary</td>
<td>• Major and minor amputation rate at index limb</td>
<td>• Mortality, independently of cause</td>
<td></td>
</tr>
</tbody>
</table>
Patient Flow

171/172 subjects enrolled

POBA
N= 86

Luminor35
N= 85

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

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


Randomization
(1:1)

6 month follow-up

12 month follow-up

* Patients with data of at least one endpoint

Data Lock: 31.08.2017

Data Lock: 31.01.2018

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</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>Luminor (iVascular)</td>
<td></td>
<td></td>
<td></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</td>
<td>0.35 [CI: 0.19; 0.79]</td>
<td>0.72 [CI: 0.68; 1.22]</td>
<td>-0.37</td>
</tr>
<tr>
<td>SeQuent Please (B. Braun)</td>
<td></td>
<td></td>
<td></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)

Follow-up (Days)

Patients with Freedom from TLR

POBA

DEB

Luminor®

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

<table>
<thead>
<tr>
<th>Improvement of Rutherford-Becker</th>
<th>after 6 months*</th>
<th>after 12 months**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel-Coated Balloon (n=74)</td>
<td>Paclitaxel-Coated Balloon (n=74)</td>
<td>Standard Angioplasty Balloon (n=72)</td>
</tr>
<tr>
<td>Deterioration of 1 stage</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>No improvement</td>
<td>10 (13.5)</td>
<td>18 (25.0)</td>
</tr>
<tr>
<td>Improvement of 1 stage</td>
<td>9 (12.2)</td>
<td>15 (20.8)</td>
</tr>
<tr>
<td>Improvement of 2 stages</td>
<td>21 (28.4)</td>
<td>19 (26.4)</td>
</tr>
<tr>
<td>Improvement of 3 stages</td>
<td>33 (44.6)</td>
<td>20 (27.8)</td>
</tr>
</tbody>
</table>
Efficacy: Improvement of Rutherford

- Asymptomatic
- Mild claudication
- Moderate claudication
- Severe claudication
- Ischemic rest pain
- Minor tissue loss

12 Months
6 Months
Baseline
DCB POBA
DCB POBA
DCB POBA

Percentage of Patients (%)
0 10 20 30 40 50 60 70 80 90 100

\[ p = 0.740^* \]

\[ p = 0.021^* \]

* Cochran-Mantel-Haenszel method was applied to compare the change of RBC at 6 and 12 months to baseline between DCB- and POBA-group
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
## Safety: Amputation after 12 months

<table>
<thead>
<tr>
<th></th>
<th>LUMINOR®</th>
<th>POBA</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor Amputation (%)</td>
<td>0 (0/85)</td>
<td>1.2 (1/86)</td>
<td>1.000</td>
</tr>
<tr>
<td>Major Amputation (%)</td>
<td>0 (0/85)</td>
<td>0 (0/86)</td>
<td>1.000</td>
</tr>
</tbody>
</table>
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
EffPac-Trial: Effectiveness of Luminor® DCB vs. POBA in the SFA: primary endpoint and 12-months results

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