The Lutonix BTK Clinical Trial Programme: Status Update and Real World Clinical Experience

Dierk Scheinert, MD
University Hospital Leipzig
Leipzig, Germany
Disclosure

Speaker name: Dierk Scheinert

I have the following potential conflicts of interest to report:

Consulting: Abbott, Angioslide, Atheromed, Biotronik, Boston Scientific, Cook Medical, Cordis, Covidien, CR Bard, Gardia Medical, Hemoteq, Intact Vascular Inc., Medtronic, Ostial Inc, TriReme Medical, Trivascular, Upstream Peripheral Technologies

Stockholder: IDEV Technologies
POBA for CLI Treatment

- 68 CLI patients due to BTK lesions
- Lesion length: 140 ± 90 mm
- **Restenosis at 3 months: 73%**

- Restenosis delays healing

*Iida O. et al. EJVES 2012; 44:425-31*

Complete ulcer healing rates
DCBs are not all the same

Technology of the In.Pact Deep Balloon: first folded and then coated

With courtesy C. I. Mena
Dry Inflate / Shake Test - SFA

• Test Articles (n = 5 each):
  - Medtronic In.Pact Admiral 6 x 60 mm
  - Lutonix 035 Drug Coated Balloon – 6 x 60 mm
  - In.Pact Amphirion Deep 3 x 80 mm

With courtesy C. I. Mena, C.R.Bard Inc.
Lutonix Coating Durability*

Simulated Clinical Use Test LUTONIX®

Amount of drug lost on the back table. (Drug measured- ng/mg)

Designed to minimize unnecessary drug exposure to staff and patients

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.
Histologic findings of emboli/vascular changes by coronary band and skeletal muscle territories in swine peripheral artery following Lutonix drug coated balloon X3 (2µg/mm² paclitaxel) dilatation at 90-days.

Loss of medial SMCs with replacement by proteoglycan/collagen.

<table>
<thead>
<tr>
<th>No.</th>
<th>No. of sections (Downstream muscle/coronary band)</th>
<th>Vascular Changes</th>
<th>Skeletal Muscle Necrosis/ Fibrosis</th>
<th>Crystalline material</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14 (12 / 2)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>14 (12 / 2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>14 (12 / 2)</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>14 (12 / 2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

5/56 (8.9%) from DCB treatment showed findings of vascular change associated with paclitaxel and/or excipient (drug carrier).

Histologic findings of emboli/vascular changes by coronary band and skeletal muscle territories in swine peripheral artery following IN.PACT ADMIRAL DCB x3 (3.5µg/mm² paclitaxel) dilatation at 90-days

38 /78 (48.7 %) from DCB treatment showed findings of vascular change associated with paclitaxel and/or excipient (drug carrier).

Skeletal Muscle: Gastrocnemius Muscle, Gluteus Maximus Muscle, Gracilis Muscle, Rectus Femoris Muscle, Semimembranosus Muscle, and Semitendinosus Muscle
Ex Vivo Administration of Fluorescent-Labeled PTX to Excised Porcine Artery

10% Oregon green labeled PTX incorporated into Lutonix DCB coating

Segment-to-segment variability ± 4.0 %
Pharmacokinetics of PTX in Arterial Tissue in a Porcine Model
Comparison In.Pact vs. Lutonix

In.Pact 3 x 3µg/mm²

C<sub>max</sub> of PTX at 3X Dose
= 66.26 ng/mg

Lutonix 2µg/mm²

C<sub>max</sub> of PTX at 1X Dose
= 58.9 ng/mg
Does Drug Coating Matter?

**Data obtained from two data sets. Virmani preclinical animal data on file. Animal test results may not be indicative of clinical performance. Different test methods may yield different results.**
German single center experience with Lutonix® DCB in BTK

presented @ LINC 2015

Sabine Steiner
Division of Interventional Angiology
University Hospital Leipzig, Germany
Study design

- Retrospective cohort study of patients undergoing below-the-knee interventions using Lutonix® drug coated balloons
- 248 patients treated, 40 lost to follow-up (16%)
- 220 limbs treated in 208 patients

Clinical follow up:
- Rate of death
- BTK re-interventions and target lesion revascularization
- Minor and major amputations
Baseline patient characteristics

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean± std</td>
<td>74.1±9.7</td>
</tr>
<tr>
<td>Female, %</td>
<td>33.8</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>77</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>69</td>
</tr>
<tr>
<td>Arterial Hypertension, %</td>
<td>95</td>
</tr>
<tr>
<td>Current/former smoking, %</td>
<td>45</td>
</tr>
<tr>
<td>Coronary heart disease, %</td>
<td>47</td>
</tr>
<tr>
<td>Cerebrovascular disease, %</td>
<td>8</td>
</tr>
</tbody>
</table>

N=208
**Interventional characteristics**

<table>
<thead>
<tr>
<th></th>
<th>N=220</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of devices used, mean± std</td>
<td>2.3±1.1</td>
</tr>
<tr>
<td>Cumulative length of devices (mm), mean± std</td>
<td>242±122</td>
</tr>
<tr>
<td>Treatment of inflow lesions, %</td>
<td>48</td>
</tr>
<tr>
<td>Femoropopliteal, %</td>
<td>29</td>
</tr>
<tr>
<td>Popliteal, %</td>
<td>19</td>
</tr>
<tr>
<td>Rutherford stage before intervention, %</td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>38.7</td>
</tr>
<tr>
<td>Stage 4</td>
<td>12.3</td>
</tr>
<tr>
<td>Stage 5</td>
<td>46.4</td>
</tr>
<tr>
<td>Stage 6</td>
<td>2.7</td>
</tr>
</tbody>
</table>
All cause death
## Follow up II – Re-interventions

<table>
<thead>
<tr>
<th></th>
<th>N=220</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTK re-intervention (including pre-planned secondary interventions), %</td>
<td>22.7</td>
</tr>
<tr>
<td>Time to 1st re-intervention (months), mean± std</td>
<td>7.6±4.8</td>
</tr>
<tr>
<td>Target lesion revascularization, %</td>
<td>15.9</td>
</tr>
<tr>
<td>Time to 1st target lesion revascularization (months), mean± std</td>
<td>8.1± 4.7</td>
</tr>
</tbody>
</table>
Freedom from target lesion revascularization

6 months: 89%
12 months: 77%
Follow up III – Amputations

- In total, 39 amputations were performed in 31 limbs (31 patients)
- From these 39 amputations were
  - 17 pre-planned minor amputations
  - 13 un-planned minor amputations
  - 9 major amputations
- All major amputations were performed in CLI patients (6.6% of the CLI cohort)
  - 6 patients with baseline Rutherford stage 5
  - 3 patients with baseline Rutherford stage 6
Freedom from major amputations

6 months: 97%
12 months: 96%
Freedom from death or major amputation

6 months: 92%
12 months: 85%
Summary

- Real world data of patients undergoing below the knee interventions using Lutonix® DCB

- Clinical follow-up indicates re-assuring effectiveness and safety profile
# Lutonix BTK Trial Summary

## PRIMARY ENDPOINTS
- Safety at 30 days
- Limb salvage & primary patency at 12 months

## NUMBER OF PATIENTS/SITES
- 480 patients at 55 global sites

## FOLLOW-UP
- **Clinical:** 1, 6, 12, 24, and 36 Months
- **Duplex Ultrasound (DUS):** 0–30 days, 6, 12, 24, & 36 months
- **Angiography in subset of patients:** 12 months
- **Telephone:** 48 and 60 Months

## NATIONAL PRINCIPAL INVESTIGATORS
- Patrick Geraghty: Washington University, St. Louis, MO
- Jihad Mustapha: Metro Health Hospital, Wyoming, MI
- Marianne Brodmann: Medical University Graz, Austria

## SPONSOR
- Lutonix Inc., Minneapolis, MN

Caution – Investigational Device, Limited by Federal (USA) Law to Investigational Use
Primary Endpoints

**SAFETY**
Freedom from Major Adverse Limb Events & All-Cause Death at 30 DAYS

- Amputation (above ankle)
- Major re-intervention
  - New bypass graft
  - Jump/Interposition graft revision
  - Thrombectomy/Thrombolysis

**EFFICACY**
Composite of Limb Salvage and Primary Patency at 12 Months

Defined as freedom from the composite of above ankle amputation, target vessel occlusion, and clinically-driven target lesion re-intervention.

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Patient Eligibility

Inclusion Criteria

• Male or non-pregnant female ≥18 years of age
• Rutherford 4-5
• Life expectancy ≥ 1 year;
• Significant stenosis (≥70%)
• A patent inflow artery
• Target vessel(s) diameter between 2 and 4 mm
• Target vessel(s) reconstitute(s) at or above the ankle

Exclusion Criteria

• Pregnant or planning on becoming pregnant
• History of stroke within 3 months
• History of MI, thrombolysis or angina within 30 days of enrollment
• Prior or planned major amputation
• GFR ≤ 30 ml/min per 1.73m²
• Acute limb ischemia
• In-stent restenosis of target lesion
BTK Trial Design

Protocol Features

- Randomized 2:1 versus POBA
- Permits treatment of two tibial arteries (two flow pathways)
- Combined lesion length of up to 32 cm treatable (36 cm balloon length allowed)
- Retrograde wire access permitted, but not retrograde intervention
- Balloon lengths of up to 12 cm
- First U.S. use of tibial patency assessment via duplex ultrasound (VasCore)
- Angiographic assessment of normal-risk subset at one year (Synvacor)
- Broad range of secondary endpoints including QOL instruments
**Inflow Treatment**
If needed

**PTA Pre-Dilatation**
With Uncoated Balloon

**Successful PTA with Outflow**

**Suboptimal PTA**
Absence of above ankle reconstitution
>75% residual stenosis

- **Test Arm:**
  Dilatation of ALL target lesions with Drug Coated Balloon

- **Control Arm:**
  Dilatation of ALL target lesions with Uncoated Balloon

Randomize 2:1

**Treat per standard practice**
30 day follow-up for safety

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What is the Data Monitoring Committee?

- Unbiased panel of leading experts in peripheral vascular disease, cardiovascular medicine and biostatistics not associated with Lutonix or the trial

- During the enrollment phase of the trial, DMC reviews accumulating safety data to monitor for incidence of serious vascular events that would warrant termination of the trial
5 Data Monitoring Committee meetings so far

172 randomized patients:
- 95 have completed 6 month follow-up
- 39 have completed 12 month follow-up

Only 5 major amputations (3% of enrolled pts) recorded

Only approved and ongoing BTK trial in the US
Summary

- There is still an unmet need for improved durability in the BTK area
- Drug-delivery via balloon-based solutions may still be the most realistic approach
- The Lutonix clinical trial programme is proceeding well – data can be expected in 2016 time frame.
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