The current role and limitations of BTK DCB: what we know now

William A. Gray MD
System Chief of Cardiovascular Services, Main Line Health
President, Lankenau Heart Institute
Wynnewood, PA
USA
What are the randomized clinical data?
Single-center, randomized, non-blinded IN.PACT Amphirion in diabetics: successful 2013

Drug-Eluting Balloon in Peripheral Intervention for Below the Knee Angioplasty Evaluation (DEBATE-BTK)
A Randomized Trial in Diabetic Patients With Critical Limb Ischemia

Francesco Liistro, MD; Italo Porto, MD PhD; Paolo Angioli, MD; Simone Grotti, MD; Lucia Ricci, MD; Kenneth Ducci, MD; Giovanni Falsini, MD; Giorgio Ventoruzzo, MD; Filippo Turini, MD; Guido Bellandi, MD; Leonardo Bolognese, MD
DEBATE BTK 12 month angiography: DCB improves patency
DEBATE BTK:
TLR improved with DCB at 12 months

Log-Rank p=0.02
Randomized multicenter trial IN.PACT DEEP: unsuccessful 2014

Drug-Eluting Balloon Versus Standard Balloon Angioplasty for Infrapopliteal Arterial Revascularization in Critical Limb Ischemia

12-Month Results From the IN.PACT DEEP Randomized Trial

Thomas Zeller, MD,* Iris Baumgartner, MD,† Dierk Scheinert, MD,‡ Marianne Brodmann, MD,§ Marc Bosiers, MD,|| Antonio Micari, MD, PhD,¶ Patrick Peeters, MD, PhD,# Frank Vermassen, MD, PhD,** Mario Landini, MS,†† David B. Snead, PhD,†† K. Craig Kent, MD,††† Krishna J. Rocha-Singh, MD,§§ IN.PACT DEEP Trial Investigators
IN.PACT DEEP: Relevant clinical outcomes

- Late Lumen Loss (mm)
- Binary restenosis (50-100%)
- Clinically-driven TLR at 12 months (AFS population)
- Major Amputation, target limb

Treatment Difference and 95% Confidence Interval
Single-center randomized DCB vs. DES: unsuccessful 2014

Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stenting for the Treatment of Infrapopliteal Long-Segment Arterial Occlusive Disease

The IDEAS Randomized Controlled Trial

Dimitris Siablis, MD, PhD,* Panagiotis M. Kitrou, MD, PhD,* Stavros Spiliopoulos, MD, PhD,* Konstantinos Katsanos, MSc, MD, PhD,† Dimitris Karnabatidis, MD, PhD*
DES better than DCB in angiographic follow-up
Interestingly, clinical outcomes not significantly different
Randomized multicenter trial BIOLUX P-II: unsuccessful
2015

Paclitaxel-Coated Balloon in Infrapopliteal Arteries
12-Month Results From the BIOLUX P-II Randomized Trial (BIOTRONIK’S-First in Man study of the Passeo-18 LUX drug releasing PTA Balloon Catheter vs. the uncoated Passeo-18 PTA balloon catheter in subjects requiring revascularization of infrapopliteal arteries)

Thomas Zeller, MD,* Ulrich Beschorner, MD,† Ernst Pilger, MD,‡ Marc Bosiers, MD,§ Koen Deloose, MD,§ Patrick Peeters, MD,|| Dierk Scheinert, MD, PHD,¶ Karl-Ludwig Schulte, MD, PHD,# Aljoscha Rastan, MD,* Marianne Brodmann, MD, PHD‡
Biolux P-II: no difference in patency

What are the causes for DCB failure?
The challenges with BTK trials: subject loss

**BIOLEX-PII**

**72 Subjects**
with infrapopliteal lesions

1:1

**DEB**
N=36

30-day FUP
N=35
Withdrawal N=1
Early Termination N=0
(Death N=0, Amputation N=0)

6-month FUP
N=30
Withdrawal N=3
Early Termination N=3
(Death N=2, Amputation N=1)

12-month FUP
N=26
Missed/ lost to FUP N=3
Withdrawal N=4
Early Termination N=3
(Death N=2, Amputation N=1)

**Uncoated balloon**
N=36

30-day FUP
N=35
Withdrawal N=0
Early Termination N=1
(Death N=0, Amputation N=1)

6-month FUP
N=33
Withdrawal N=0
Early Termination N=3
(Death N=1, Amputation N=2)

12-month FUP
N=30
Missed/ lost to FUP N=2
Withdrawal N=0
Early Termination N=4
(Death N=2, Amputation N=2)

56 (78%)

**IN.PACT DEEP**

358 enrolled

358 randomized

**DEB**
n = 239

30-day follow-up
n = 203

16 died
8 withdrew
14 major amputation
1 lost to follow-up
19 no follow-up

6-month follow-up
n = 182

24 died
14 withdrew
20 major amputation
1 lost to follow-up
16 no follow-up

12-month follow-up
n = 165

256 (72%)

**PTA**
n = 119

30-day follow-up
n = 110

6 died
3 withdrew
3 major amputation
1 died + major amp.
0 lost to follow-up
7 no follow-up

6-month follow-up
n = 94

6 died
3 withdrew
3 major amputation
1 died + major amp.
2 lost to follow-up
6 no follow-up

12-month follow-up
n = 91
IN.PACT DEEP: Root Cause Analysis

Key Factors:
1. Older technology (balloon material) provided insufficient drug delivery
2. Trial enrolled high risk subjects predisposed to safety event independent of intervention

Contributing Factors / Additional Points of Interest:
1. Procedural differences between study arms led to higher rate of procedural complications in DCB
2. Inadequate sample size and excessive loss of follow-up
3. The DCB major amputation rate was consistent with historical data and there were no unusual events caused by IN.PACT™ Amphirion™
4. Unprecedented, favorable PTA major amputation rate
Is calcium really the problem?
Calcium not prominent in failed trials

**Table 3:** Baseline Angiographic and Procedural Characteristics (ITT Population)

<table>
<thead>
<tr>
<th></th>
<th>IA-DEB</th>
<th>PTA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length, cm</td>
<td>10.15 ± 9.10</td>
<td>12.86 ± 9.46</td>
<td>0.002</td>
</tr>
<tr>
<td>Lesion length in angiography cohort, cm</td>
<td>5.91 ± 4.17</td>
<td>7.97 ± 7.46</td>
<td>0.060</td>
</tr>
<tr>
<td>Reference vessel diameter, mm</td>
<td>2.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total occlusions</td>
<td>38.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restenotic lesions</td>
<td>6.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe calcium</td>
<td>13.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** Lesion Characteristics at Baseline and Follow-Up Per Core Laboratory Assessment

<table>
<thead>
<tr>
<th></th>
<th>Baseline*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>DEB</td>
</tr>
<tr>
<td>Lesion location</td>
<td></td>
</tr>
<tr>
<td>Anterior tibial artery</td>
<td>24 (48.0)</td>
</tr>
<tr>
<td>Posterior tibial artery</td>
<td>11 (22.0)</td>
</tr>
<tr>
<td>Peroneal artery</td>
<td>7 (14.0)</td>
</tr>
<tr>
<td>Tibioperoneal trunk</td>
<td>5 (10.0)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (6.0)</td>
</tr>
<tr>
<td>Calcification†</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>19 (55.9)</td>
</tr>
<tr>
<td>Mild</td>
<td>6 (17.6)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Moderate/severe</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Severe</td>
<td>5 (4.7)</td>
</tr>
</tbody>
</table>
What now?
Lutonix DCB Versus Standard Balloon Angioplasty for Treatment of Below-The-Knee (BTK) Arteries

**This study is currently recruiting participants.** *(see Contacts and Locations)*

**Verified May 2016 by C. R. Bard**

**Sponsor:**
C. R. Bard

**Collaborator:**
Bard Ltd

**Information provided by (Responsible Party):**
C. R. Bard

**ClinicalTrials.gov Identifier:**
NCT01870401

First received: May 7, 2013
Last updated: May 25, 2016
Last verified: May 2016

**Tracking Information**

<table>
<thead>
<tr>
<th>First Received Date</th>
<th>May 7, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last Updated Date</td>
<td>May 25, 2016</td>
</tr>
<tr>
<td>Start Date</td>
<td>May 2013</td>
</tr>
</tbody>
</table>
Future trials

Tensirolimus Adventitial Delivery to Improve Angiographic Outcomes Below the Knee (TANGO) (TANGO)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified September 2016 by Mercator MedSystems

Sponsor:
Mercator MedSystems, Inc.

Information provided by (Responsible Party):
Mercator MedSystems, Inc.
Conclusions

• DES and DCBs promise to become the therapy of choice for the treatment of symptomatic SFA disease

• There remains a paucity of randomized, multicenter, blinded study data to support DCB use BTK

• Newer trials and technological improvements/evolution will hopefully provide these data
The current role and limitations of BTK DCB: what we know now

William A. Gray MD
System Chief of Cardiovascular Services, Main Line Health
President, Lankenau Heart Institute
Wynnewood, PA
USA