Dedicated Bifurcation Optimization Stent System – First-In-Human Results

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I have the following financial relationships to disclose:

Consultancy: Balton, PL

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Bifurcations - main treatment problems

- Periprocedural complications – side branch significant stenosis occurrence and occlusion after main vessel stenting
- Increased long-term restenosis and reintervention`s number
- Increased risk of stent thrombosis
Problems with current dedicated bifurcation stents

- None of currently dedicated stents does not fit bifurcation anatomy according to optimality principles.
- Neither dedicated stent does not eliminate the basic mechanism for SB compromise – carina displacement.
- All stents, crossing the bifurcation segments confluent point are difficult to implant, because are tracked over 2 wires, which poses significant problems.
1. Delivery system is based on dedicated balloon (Bottle®, Balton, PL) which restore MV – MB sizes without need of additional dilatation (kissing like effect)

2. It’s profile is quite low (1.08mm), which makes possible to implant stent even through 5 Fr guiding catheter

3. Two parts of stent (dedicated for MV and MB) made of 316L stainless steel are connected with two struts at the step-up mid zone – it keeps SB ostial diameter

4. Balloon mid-marker allows exact stent positioning
BiOSS® (Balton, PL)

4. The stent construction prevents carina displacement, as a basic mechanism of side branch compromise

5. The stent strut/vessel area ratio varies between 15 – 18%. Nominal foreshortening of the stent is less than 0.5%.

6. Stent belongs to DES class – biodegradable polimer with paclitaxel (BiOSS® Expert Bis)
**BiOSS – CREATED ON THE BASE OF LUC-CHOPIN²**

**STENT - FIRST DES WITH BIODEGRADABLE POLYMER**

**PLGA CO-POLYMER**

**Physical Properties**
- Combination of polilactide and polyglycolyc polymers
  - Inert
  - Flexible, ductable
  - Thin, with high drug loading capacity

**Mechanical integrity**
- Strong adhesion to stent

**Manufacturability**
- High stability of the manufacture process

**Luc-Chopin²: PLGA Co-polymer**
- Controlled degradation time = controlled drug release

**Biocompatibility**
- Low thrombogenicity and inflammation
  (Polylactide and poliglycolye is physiologically present in human body)

**Manufacturability**
- High stability of the manufacture process

**Controlled degradation time = controlled drug release**

**PLGA degrades in 8 weeks releasing CO₂ and H₂O only**
How BiOSS works?

BiOSS after balloon deflation, copies the bifurcation configuration matching proximal – distal main vessel size requirements. It fits all parts of bifurcation (parent vessel – daughter branches) according to principles of optimality of energy distribution in coronary artery branching region (Murray law).
BiOSS in IVUS
BiOSS Registry
safety and feasibility study

• Primary end-point
  – MACE event rates at 12 months

• Secondary end-points
  – Device performance – implantation failure rates
  – Periprocedural safety – rate of periprocedural SB compromise (SB closure rates, elev. CK-MB)
  – Angiographic (after 9 months):
    • Late Lumen Loss (LL)
    • Percent Diameter Stenosis (%DS)
    • Binary restenosis rate
Centres participating in BiOSS® Registry

- Robert J. Gil – CSK MSWiA, Warsaw, Poland – PI of BiOSS Registry
- Dobrin Vassilev - CSK MSWiA, Warsaw, Poland
- Adam Kern - WSS, Olsztyn, Poland
- Radoslaw Formuszewicz - KKKCW UMK, Bydgoszcz, Poland
- Slawomir Dobrzycki - KKI USK, Bialystok, Poland
- Maciej Lesiak - I KK SKiPP, Poznan, Poland
- Jaroslaw Wojcik - KK SPSK, Lublin, Poland
- Piotr Kardaszewicz - WSS, Czestochowa, Poland
- Mariusz Gasior – SCCS, Zabrze, Poland
- Jozef Jodkowski – WIM, Warsaw
Methods

• Inclusion criteria
  – All patients with all types coronary bifurcation stenosis without STEMI
  – Able to take 12 month DAP
  – Serum creatinine <2.0 mg/dl

• Exclusion criteria
  - lack of informed consent & STEMI

No vessel location restrictions – LM included!
BiOSS implantation protocol

- Wiring both branches
- MV predilatation (B/A ratio = 0.8 – 1.0)
- SB predilatation according to operator decision
- BiOSS implantation – 10-12 atm at least 20 sec!
- Stent postdilatation – Bottle balloon
- SB postdilatation if SB ostial %DS >70% (operator decision, not mandatory per protocol)
- KBI not required!
- IVUS mandatory for all LM cases
### Demographic characteristics, n=63

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67 ± 11</td>
</tr>
<tr>
<td>Sex – males</td>
<td>38 (63)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>31 (52)</td>
</tr>
<tr>
<td>NSTEMI / Unstable angina</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35 (58)</td>
</tr>
<tr>
<td>Elevated cholesterol / statin treatment</td>
<td>24 (40)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>16 (27)</td>
</tr>
<tr>
<td>Smoking</td>
<td>6 (10)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>18 (30)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>24 (38)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>6 (10)</td>
</tr>
</tbody>
</table>
Medina types

XX1 = 70%!
Number of diseased vessels

1 VI: 16%  
2 VI: 48%  
3 VI: 16%  
LM: 20%

Target lesion location

LM: 20% (13)  
LAD: 54% (35)  
LCX: 23% (15)  
RCA - PD/PL: 2% (1)
RESULTS

- 63 pts, 9 high volume (>1500 PCIs/year) Polish centers
- 65 bifurcation lesions
- 65 BiOSS stents implanted

100% device success rate!
## Procedural characteristics

<table>
<thead>
<tr>
<th>Affected vessel - lesions</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV predilatation</td>
<td>78%</td>
</tr>
<tr>
<td>SB predilatation</td>
<td>26%</td>
</tr>
<tr>
<td>Predilatation of both branches</td>
<td>15 (24)</td>
</tr>
<tr>
<td><strong>Stent diameter, mm - MV</strong></td>
<td>3.60 ± .22</td>
</tr>
<tr>
<td><strong>Stent diameter, mm - MB</strong></td>
<td>2.83 ± .22</td>
</tr>
<tr>
<td><strong>Stent length, mm</strong></td>
<td>17±2</td>
</tr>
<tr>
<td>Implantation pressure, atm.</td>
<td>14 ± 1</td>
</tr>
<tr>
<td>Sequential balloon inflation</td>
<td></td>
</tr>
<tr>
<td>MV</td>
<td>33 (61)</td>
</tr>
<tr>
<td>SB</td>
<td>36 (58)</td>
</tr>
</tbody>
</table>
Procedural characteristics

- **FINAL KISSING BALLOON INFLATION**: 8/65 (12%)
- **BOTTLE BALLOON POSTDILATATION**: 17/65 (26%)
- **SB BALLOON POST DILATATION**: 34/65 (52%)
- Additional stent in SB – 6 pts (5 LM)
- Additional stent in MV/MB – 19 pts
## Angiographic characteristics

### whole group

<table>
<thead>
<tr>
<th>Angiographic characteristics</th>
<th>Before stent</th>
<th>After stent</th>
<th>p – value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main vessel</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV – RVD, mm</td>
<td>3.41 ± 0.51</td>
<td>3.46 ± 0.36</td>
<td>NS</td>
</tr>
<tr>
<td>MV - % DS</td>
<td>49% ± 15%</td>
<td>8% ± 13%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td><strong>Main branch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main branch – RVD, mm</td>
<td>2.72 ± 0.49</td>
<td>2.79 ± 0.37</td>
<td>NS</td>
</tr>
<tr>
<td>MB - %DS</td>
<td>51% ± 11%</td>
<td>2% ± 18%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>MB lesion length, mm</td>
<td>16 ± 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side branch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SB – RVD, mm</td>
<td>2.39 ± 0.45</td>
<td>2.34 ± 0.41</td>
<td>NS</td>
</tr>
<tr>
<td>SB - %DS</td>
<td>55% ± 21%</td>
<td>63% ± 16%</td>
<td>NS</td>
</tr>
<tr>
<td>SB - %DS – final, mm</td>
<td></td>
<td>39% ± 21%</td>
<td></td>
</tr>
<tr>
<td>SB lesion length, mm</td>
<td>4.1 ± 1.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Angle alpha, degrees</strong></td>
<td>40 ± 15</td>
<td>39 ± 16</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Angle A, degrees</strong></td>
<td>58 ± 18</td>
<td>53 ± 17</td>
<td>P = 0.04</td>
</tr>
</tbody>
</table>
30 day results – 63 pts

• Death – 0%

• Myocardial infarction
  – In-hospital (periprocedural)
    • 6/63 (9.5%)
      » n=1 (1.5%) increased Tn + CK-MB (non-Q MI)
      » n=5 (7.8%) increased Tn only, no change in CK, CKMB
  – Out of hospital – 0%

• TLR – 0%

• TVR – 0%

• PCI in another vessel – 1 (1.6%)
Cumulative clinical results – 12 month (out of hospital)

- **Death** – 2/63 (3.2%): 1\textsuperscript{st} - 3 months after index PCI - LAD/D
  2\textsuperscript{nd} – 10 months after PCI – LM/LAD
- **Myocardial infarction** – 0%
- **Stroke** – 0%
- **ST** – 0%
- **TLR** – 7/63 (11%): 3x CABG, 2x POBA, 2x Stent
- **TVR** – 9/63 (14.3%)
- **Comp. MACE** (death, MI, stroke, TVR) – 9/63 (14.3%)
- **PCI in other vessel not related with BiOSS vessel** – 15/63 (23.8%)
QCA results: In-segment restenosis location
QCA analysis - Changes in %DS

**MV**
- Pre: 46, Post: 8, FU: 21
- p < .001

**MB**
- Pre: 55, Post: 2, FU: 19
- p < .001

**SB**
- Pre: 57, Post: 39, FU: 25
- p = .033
### QCA analysis - Change in MLD

<table>
<thead>
<tr>
<th></th>
<th>MV</th>
<th>MB</th>
<th>SB</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre</td>
<td>1.85</td>
<td>1.47</td>
<td>1.32</td>
</tr>
<tr>
<td>post</td>
<td>3.13</td>
<td>2.65</td>
<td>1.47</td>
</tr>
<tr>
<td>FU</td>
<td>2.75</td>
<td>2.28</td>
<td>1.75</td>
</tr>
</tbody>
</table>

- MV: *p* < 0.001
- MB: *p* < 0.001
- SB: *p* = 0.017
QCA analysis: Late loses in LM and non-LM groups

Non LM

- MV LLL: 0.34, p = .041
- MB LLL: 0.52, p = .001
- SB LLL: -0.05

LM

- MV LLL: 0.58
- MB LLL: 0.26, p = .001
- SB LLL: 0.09

All p non significant
Conclusions

• Simple and fast bifurcation treatment with single dedicated paclitaxel eluting bifurcation stent is feasible and highly successful (100% implantation rate)
• In-stent long term results are very satisfactory
• The initial short length of the device inflate TVR rates, because of missed edge dissections
• Minimalistic strategy for treatment of diseased side branches needs reconsideration
• The long-term results MACEs inflated, because of very risk profile of patient population
EC Design-Examination Certificate
No. 11 0052 CN/NB

issued in compliance with the Council Directive 93/42/EEC as amended, which is implemented by the Czech Government Order No. 398/2004 (Collection of Laws) certifies that the product – medical device of Class III, type
PAACLITAXEL ELUTING CORONARY BIFURCATION STENT
“BIOSSE Expert” WITH DELIVERY SYSTEM, RAPID EXCHANGE

manufactured by company
Balton Sp. z o.o.
Nowy Świat 7/14, 00-496 Warszawa, Poland

fulfills the essential requirements specified in the Annex I of the Directive 93/42/EEC relating to it, taking into account the product’s intended use.
The Notified Body No. 1023 has executed the EC design-examination of the above-mentioned product according to the Annex II, paragraph 4, of the Directive 93/42/EEC. The detailed product descriptions, documents, assessment procedures and evaluation of the examination are presented in the Final Report No. 80390906752011, which is enclosed to this Certificate.

The Certificate is issued under the following conditions:
1. It applies only to the design of the above referenced models of the medical devices.
2. It does not imply that the Notified Body has performed any surveillance or control of their manufacture.
3. The manufacturer is obligated to assure that all medical devices of the respective models conform to the type whose design has been approved by this Certificate.
4. The Certificate remains valid until the approved design is changed but until the 26th January 2016 at the latest.
5. After receiving the complementary EC Certificate, confirming the manufacturer’s quality system approval by the Notified Body No. 1023, and fulfilling the relevant EU legislation, the manufacturer shall affix to each medical device, of the above referenced models, the CE-marking followed by the number of the Notified Body according to this example:

CE 1023

Issued in Zlin on 26th January 2011
Representative of the Notified Body No. 1023
Thank you!
## Angiographic characteristics

**LM group (13 pts)**

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<td><strong>Main vessel</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MV – RVD, mm</td>
<td>3.86 ± 0.42</td>
<td>3.85 ± 0.26</td>
<td>NS</td>
</tr>
<tr>
<td>MV - % DS</td>
<td>43% ± 19%</td>
<td>8% ± 12%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td><strong>Main branch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main branch – RVD, mm</td>
<td>3.06 ± 0.17</td>
<td>3.00 ± 0.21</td>
<td>NS</td>
</tr>
<tr>
<td>MB - %DS</td>
<td>52% ± 12%</td>
<td>7% ± 14%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>MB lesion length, mm</td>
<td>14 ± 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side branch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SB – RVD, mm</td>
<td>2.93 ± 0.41</td>
<td>2.78 ± 0.21</td>
<td>NS</td>
</tr>
<tr>
<td>SB - %DS</td>
<td>61% ± 22%</td>
<td>61% ± 19%</td>
<td>NS</td>
</tr>
<tr>
<td>SB - %DS – final, mm</td>
<td></td>
<td>20% ± 12%</td>
<td></td>
</tr>
<tr>
<td>SB lesion length, mm</td>
<td>4.3 ± 1.60</td>
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</tbody>
</table>
# Angiographic characteristics
non – LM group (50 pts)

<table>
<thead>
<tr>
<th>Angiographic characteristics</th>
<th>Before stent</th>
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<th>p – value</th>
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<tbody>
<tr>
<td><strong>Main vessel</strong></td>
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<td></td>
</tr>
<tr>
<td>MV – RVD, mm</td>
<td>3.26 ± 0.30</td>
<td>3.33 ± 0.16</td>
<td>NS</td>
</tr>
<tr>
<td>MV - % DS</td>
<td>49% ± 15%</td>
<td>3% ± 11%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td><strong>Main branch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main branch – RVD, mm</td>
<td>2.61 ± 0.31</td>
<td>2.73 ± 0.28</td>
<td>NS</td>
</tr>
<tr>
<td>MB - %DS</td>
<td>66% ± 12%</td>
<td>9% ± 12%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>MB lesion length, mm</td>
<td>16 ± 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side branch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SB – RVD, mm</td>
<td>2.41 ± 0.42</td>
<td>2.39 ± 0.47</td>
<td>NS</td>
</tr>
<tr>
<td>SB - %DS</td>
<td>59% ± 21%</td>
<td>63% ± 16%</td>
<td>NS</td>
</tr>
<tr>
<td>SB - %DS – final, mm</td>
<td></td>
<td><strong>31% ± 19%</strong></td>
<td></td>
</tr>
<tr>
<td>SB lesion length, mm</td>
<td>4.0 ± 1.45</td>
<td></td>
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</tbody>
</table>
9-12 months angiographic results

Minimal lumen diameter

- 1.74 ± 0.62 mm
- 2.38 ± 0.59 mm
- 2.75 ± 0.62 mm
9-12 months angiographic results

%DS

21% ± 16%

25% ± 21%

19% ± 21%
9-12 months angiographic results
Late lumen loss

-0.01 ± 0.68 mm

0.39 ± 0.54 mm

0.43 ± 0.59 mm