Long-term Outcome of Biodegradable Compared to Durable Polymer Drug-Eluting Stents and Bare Metal Stents – Main Results of a Prospective Randomized Trial

- the BASKET PROspective Validation Examination II-

(BASKET-PROVE II)

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supported by the Basel Cardiovascular Research Foundation

➢ no industry involvement in design, analysis or interpretation of data

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Background

⇒ Promise of biodegradable-polymer drug-eluting stents (BP-DES) to be as:

- effective as 2nd generation durable-polymer drug-eluting stents (DP-DES)
- safe >1 year as bare-metal stents (BMS), i.e. very late stent thrombosis (VLST) due to persistent polymers should no longer appear

Aims

⇒ To compare the long-term performance of a BP-DES to
- the most widely used 2nd generation DP-DES
- a last-generation thin-strut coated BMS
Study Design I

Inclusion: 2'291 patients in need of >3.0mm stents irrespective of clinical indication for PCI/stent (April 2010 until May 2012)

Exclusions: shock, in-stent restenosis, stent thrombosis, unprotected LM or SVG, planned surgery < 12 months, oral anticoagulation / increased bleeding risk, history of TIA or stroke, stents >4mm, no compliance

Randomization 1:1:1 to

Biolimus-eluting BP-DES (Nobori ®) vs
Everolimus-eluting DP-DES (Xience-PRIME ®) vs
thin-strut coated Cobalt-Chromium BMS (Prokinetik ®)
Study Design II

Assumptions:  
- 2-year primary EP for DP-DES: 7.6% (BASKET-PROVE, NEJM 2010)
- Non-inferiority margin: 3.8%

Sample Size:  
- 2x800 patients (incl. 10% lost-to-follow-up) for non-inferiority, power 80%, at one-sided type I error of 0.05

DAPT:  
- ASS and Prasugrel for all patients
  - 12 months after DES or ACS, 4 weeks after elective BMS
  - Prasugrel: 60mg loading-dose, 10mg daily (5mg >75 years or <60kg)

Follow-up:  
- 24 months, angio for clinical indication only

Endpoints:  
- 1° EP: Efficacy: MACE (cardiac death/MI/TVR) within 2 years
  a) BP-DES vs DP-DES (non-inferiority)
  b) BP-DES vs BMS (superiority)
- 2° EP: Safety: = definite/probable ST/MI/cardiac death
  - late = > 1 year
Patient Flow

2',299 patients randomized
- 8 refused definite consent
2',291 patients included

765 allocated to BP-DES
- 746 FU-information for primary EP available
  - 19 censored at time-point of refusal or loss to follow-up
  - 765 analyzed for primary EP

765 allocated to DP-DES
- 748 FU-information for primary EP available
  - 17 censored at time-point of refusal or loss to follow-up
  - 765 analyzed for primary EP

761 allocated to BMS
- 745 FU-information for primary EP available
  - 16 censored at time-point of refusal or loss to follow-up
  - 761 analyzed for primary EP

• Survival status known after 2 years: 98.5%
• Complete follow-up after 2 years: 97.7%
# Baseline Characteristics

## BASKET-PROVE II

<table>
<thead>
<tr>
<th></th>
<th>BP-DES</th>
<th>DP-DES</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients n</td>
<td>765</td>
<td>765</td>
<td>761</td>
</tr>
<tr>
<td>Male (%)</td>
<td>78</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62±11</td>
<td>62±11</td>
<td>63±11</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>21</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>66</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Hypercholesterol (%)</td>
<td>65</td>
<td>63</td>
<td>62</td>
</tr>
<tr>
<td>Current Smoker (%)</td>
<td>35</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>9</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Prior PCI (%)</td>
<td>13</td>
<td>12</td>
<td>15</td>
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<tr>
<td>Prior CABG (%)</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Stable Angina (%)</td>
<td>36</td>
<td>35</td>
<td>39</td>
</tr>
<tr>
<td>UA/NSTEMI (%)</td>
<td>34</td>
<td>35</td>
<td>33</td>
</tr>
<tr>
<td>STEMI (%)</td>
<td>30</td>
<td>29</td>
<td>27</td>
</tr>
</tbody>
</table>

(No significant differences between groups)
## Baseline Vessel Disease and Intervention

<table>
<thead>
<tr>
<th></th>
<th>BP-DES</th>
<th>DP-DES</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>765</td>
<td>765</td>
<td>761</td>
</tr>
<tr>
<td>MV- disease (%)</td>
<td>37</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>LAD treated (%)</td>
<td>62</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>Bifurcations treated (%)</td>
<td>4</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>CTO treated (%)</td>
<td>4</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>GP IIb/IIIa blockers (%)</td>
<td>12</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td># of stented lesions/patient</td>
<td>1.2±0.5</td>
<td>1.3±0.6</td>
<td>1.3±0.5</td>
</tr>
<tr>
<td># of stents/patient</td>
<td>1.5±0.8</td>
<td>1.5±0.9</td>
<td>1.5±0.8</td>
</tr>
<tr>
<td>total stent length/pat. (mm)</td>
<td>26±17</td>
<td>27±18</td>
<td>25±16</td>
</tr>
<tr>
<td>Angiographic success (%)</td>
<td>96</td>
<td>96</td>
<td>95</td>
</tr>
</tbody>
</table>

(No significant differences between groups)
Primary Endpoint

**cardiac death/MI/TVR**

**BP-DES versus DP-DES**

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HR 1.11; CI 0.77-1.62, p=0.58
Non-Inferiority Analysis

BP-DES versus DP-DES

**ITT-Population**

Intention to treat: absolute risk difference 0.75% (95%CI -1.93% to 3.50%, p for non-inferiority: **0.04**)

**PP-Population**

Per protocol: absolute risk difference 1.41% (95%CI 1.33% to 4.15%, p for non-inferiority: **0.09**)

*Difference due to exclusion of 6 events in patients with protocol violations: 4 due to DAPT violations, 2 no stent*
Key Safety Secondary Endpoint

Cardiac Death / MI / def. or prob. ST

BP-DES versus BMS

HR: 0.72; CI 0.44-1.18

No difference in late safety
Comparison of all 3 Stent Groups
Early vs Late Events

**Efficacy**
Card death/MI/TVR

**Safety**
Card death/MI/def/prob ST

* p<0.001
Discussion

⇒ BP-II was powered for *efficacy*, the primary EP (i.e. non-inferiority), not for *late safety*
  - >20’000 patients needed to prove significant differences in VLST

⇒ The non-inferiority margin was 3.8%
  - In accordance with previous trials

⇒ All patients were treated with *prasugrel*-based DAPT
  - May question the generalizability of the results on VLST and ischemic endpoints (separate analysis under review)

⇒ Results apply for patients with *large vessel* stenting
  - Selected for low TVR-, high MI/death-risk
Conclusions and Implications

⇒ By intention-to-treat, biolimus-eluting BP-DES were non-inferior to everolimus-eluting DP-DES after 2 years in a real-world population of patients in need for large-vessel stenting.

⇒ Both DES were superior in efficacy (TVR↓) to thin-strut coated BMS.

⇒ There was no evidence for a better safety, particularly a lower very late stent thrombosis rate, for BP-DES beyond 1 year.

⇒ Findings challenge the concept that polymers should be key in the perceived late deficiency (VLST↓) of DP-DES.