Impact of chronic renal failure on safety and effectiveness of paclitaxel-eluting stents: 2-year results from the Zilver PTX Post-Market Surveillance Study in Japan

Yukihiisa Ogawa, MD.
Department of Radiology
St. Marianna University School of Medicine, Japan
Disclosures

I have no COI with regard to our presentation.
Zilver PTX® Drug-Eluting Stent

• Designed for the SFA
• Paclitaxel only
  – No polymer or binder
  – 3 µg/mm² dose density
• Zilver Flex® Stent Platform
Global Clinical Program

Pre-Market Studies

- **RCT**
  - Moderate lesions
    - PTA
      - Optimal n=118
      - Sub-optimal
        - Zilver Flex n=56
        - Zilver PTX n=63
        - Zilver PTX n=787
        - Zilver PTX n=175

- **SAS**
  - More complex lesions
    - Zilver PTX n=242

- **China**
  - Similar lesions to RCT

Post-Market Studies

- **Japan**
  - PMS
    - All-comers
      - Zilver PTX n=905

- **US PAS**
  - Similar lesions to RCT
    - Zilver PTX n=200

- **EU**
  - Longer Lesions
    - Zilver PTX n=45

More than 2400 patients to be included in current Zilver PTX clinical program
## Global Clinical Program

<table>
<thead>
<tr>
<th>Key Study Criteria</th>
<th>Zilver PTX RCT</th>
<th>Zilver PTX SAS</th>
<th>Zilver PTX Japan PMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No significant untreated inflow tract stenosis</td>
<td></td>
<td>ALL patients treated with Zilver PTX enrolled (up to enrollment limit), No exclusion criteria</td>
</tr>
<tr>
<td></td>
<td>At least one patent runoff vessel</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Maximum 2 Zilver PTX stents per lesion</td>
<td>Maximum 4 Zilver PTX stents per patient</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lesion length ≤ 14 cm</td>
<td>No exclusions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>One lesion per limb</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No prior stent in SFA</td>
<td>ISR included</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Excluded if serum creatinine &gt; 2.0, renal failure, or dialysis</td>
<td>No exclusions</td>
<td></td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>Clopidogrel or ticlopidine recommended for 60 days, aspirin indefinitely</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>5 years</td>
<td>2 years</td>
<td>5 years</td>
</tr>
<tr>
<td>Patency</td>
<td>DUS core laboratory analysis</td>
<td>DUS site analysis</td>
<td></td>
</tr>
<tr>
<td>Stent Integrity</td>
<td></td>
<td>X-ray core laboratory analysis</td>
<td></td>
</tr>
</tbody>
</table>

Increasingly complex patients and lesions
Freedom from TLR from Global Studies

Japan PMS TLR rate consistent with pre-market studies despite more complex lesions
Clinical Benefit from Global Studies

Clinical benefit in the Japan PMS is similar to both pre-market studies.
Summary of 3-year JPMS Results

• Japan PMS included a challenging patient population with complex lesions
  – 35% of patients had chronic renal failure (CRF)

• 3-year Japan PMS results are positive and continue to support the long-term benefit of the Zilver PTX technology
Subgroup Analysis of Chronic Renal Failure Patients from the Japan PMS

Japan PMS
n = 905

Enrollment

Chronic renal failure (CRF) n = 321

No chronic renal failure (non-CRF) n = 584

2-year data available

n = 209

n = 453

CRF was defined as eGFR < 60 mL/min/1.73m² and/or dialysis
### Patient Demographics and Comorbidities

<table>
<thead>
<tr>
<th></th>
<th>CRF</th>
<th>Non-CRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>321</td>
<td>584</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>72 ± 9</td>
<td>74 ± 8</td>
</tr>
<tr>
<td>Male</td>
<td>68%</td>
<td>72%</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>69%</td>
<td>53%</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>57%</td>
<td>63%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>86%</td>
<td>85%</td>
</tr>
<tr>
<td>Pulmonary disease*</td>
<td>6%</td>
<td>9%</td>
</tr>
</tbody>
</table>

* p<0.05

Higher incidence of diabetes and pulmonary disease in the CRF group
## Baseline Lesion Characteristics

<table>
<thead>
<tr>
<th></th>
<th>CRF</th>
<th>Non-CRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions</td>
<td>381</td>
<td>699</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>146 ± 93</td>
<td>147 ± 98</td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td>91 ± 10</td>
<td>92 ± 11</td>
</tr>
<tr>
<td>Total occlusions*</td>
<td>34%</td>
<td>45%</td>
</tr>
<tr>
<td>In-stent restenosis</td>
<td>17%</td>
<td>20%</td>
</tr>
<tr>
<td>Severe calcification*</td>
<td>32%</td>
<td>9%</td>
</tr>
<tr>
<td>CLI; Rutherford (≥4) *</td>
<td>33%</td>
<td>15%</td>
</tr>
<tr>
<td>Patent runoff vessels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>1</td>
<td>35%</td>
<td>30%</td>
</tr>
<tr>
<td>&gt;2</td>
<td>58%</td>
<td>63%</td>
</tr>
</tbody>
</table>

* $p<0.05$

Higher rates of severe calcification and CLI in the CRF group
Safety

• No device or procedure related deaths

• 1249 stents implanted
  – 0.5% fracture rate in CRF group through 1 year
  – 3.7% fracture rate in non-CRF group through 1 year

• Through 2 years, low rate of thrombosis

• Through 2 years, 8 patients in the CRF group (2.5%) and 2 patients in the non-CRF group (0.3%) had an amputation
  – Four of these occurred within 2 months from the initial procedure likely reflecting a more advanced stage of PAD
Freedom from TLR rates are similar through 2 years

P=0.24 (Log-Rank)
Primary patency rates are similar through 2 years
Clinical Benefit

Clinical benefit rates are similar through 1 year but lower in the CRF group through 2 years.

Clinical benefit is defined as freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss.

P<0.01 (Log-Rank)
Conclusions

• First comparative analysis of Zilver PTX in patients with and without CRF
  – More complex lesions in the CRF group

• Zilver PTX of CRF patients is safe and effective with similar patency and TLR rates compared to patients without CRF
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