Regulatory Issues for PAD Devices

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I, (Koji Ikeda) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Current Situation of PAD Treatments in Japan

• SFA
  - Increasing number of patients
  - Progressive disease, Poor prognosis
  - Intravascular treatment: Balloon angioplasty (SFA stent is still not approved in Japan)

• BTK
  - Increasing number of patients
  - Progressive disease, Poor prognosis
  - Intravascular treatment: Balloon angioplasty

There is an urgent need of intravascular devices for PAD.
# Points of Designing Trial for PAD

<table>
<thead>
<tr>
<th></th>
<th>SFA</th>
<th>BTK</th>
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<tbody>
<tr>
<td><strong>Targeted Pts of</strong></td>
<td>TASK II, Type A and B</td>
<td>Stenosis length ?</td>
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<tr>
<td><strong>Intravascular</strong></td>
<td>Fontaine II -</td>
<td>*Criteria is not clear</td>
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<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
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<td><strong>Objective of</strong></td>
<td>Remission of intermittent claudication</td>
<td>Rutherford 4: pain relief</td>
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<td><strong>Therapy</strong></td>
<td></td>
<td>Rutherford 5 ≤ : ulcer healing, avoidance of amputation</td>
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<td><strong>Control in Clinical</strong></td>
<td>Balloon angioplasty</td>
<td>Balloon angioplasty</td>
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<tr>
<td><strong>Trial</strong></td>
<td></td>
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<td><strong>Primary Endpoint</strong></td>
<td>Primary patency</td>
<td>Clinical endpoint?</td>
</tr>
<tr>
<td><strong>Evidence for SOC</strong></td>
<td>Balloon angioplasty: insufficient</td>
<td>Balloon angioplasty: insufficient</td>
</tr>
<tr>
<td><strong>in Japan</strong></td>
<td>Bypass surgery: insufficient</td>
<td>Bypass surgery: insufficient</td>
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</tbody>
</table>

*Relatively-simple in SFA, but many obstacles for BTK*
Issues in Reviewing Other Countries’ Trials for SFA Region

• Insufficient evidence of SOC as historical control
  → Obscureness in objective of therapy

• Extrapolability of other countries’ trials
  - complexity of clinical state
  - lifestyle (sitting position, total walking time, etc.)
  - care setting (drugs, devices, SOC)
  - influencing factors to efficacy and safety are not clear

*Limitation of extrapolability*

→ *Japanese clinical data is required*
Points of Designing Trials for BTK

• Targeted Patients
  - High population of hemodialysis (HD) patients
  - High population of elderly patients
  - Criteria for amputation is different: Japanese population includes patients who are applied amputation
  - Rutherford 4 and 5+ can be evaluated by the same endpoints?

• Patency can be a surrogate endpoint?
  - Patency may not reflect AFS improvement
  - What is a suitable endpoint?

Composite endpoint is required?
Points of Designing Trials for BTK

- Insufficient evidence of Japanese population with SOC
  (both in distal bypass & intravascular treatment)
- Difference in targeted patient population
- Need to re-examine endpoints
- Limitation of extrapolability
  - different patient population
  - care setting (drugs, devices, SOC)

Limitation of extrapolability
→ Japanese clinical data is required
Summary and Future Plan

• Japanese clinical results is being accumulated from clinical trails for SFA devices
  → Raising the possibility of standardization with trials in other countries

• Clear distinction with targeted patient population. Need to re-examine endpoints.
  → Need more discussion in expert meetings with industry/academia/government with transparency
  → To facilitate mutual understanding of the distinction and stimulate developments are important
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Thank you!