Regulatory Issues for PAD Devices

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Disclosure Statement of Financial Interest

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

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

***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 efficay 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!