A Pharmaceutical Company's View on Investigator Initiated Clinical Research/Trial with Unapproved Drugs

研究者主導未承認薬臨床試験に対する企業の考え方

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Objective

To discuss how Japan sites can conduct Investigator Initiated Clinical Research/Trials (IITs) using unapproved drugs at an early stage
Agenda

- Why have IITs at an early stage not been conducted in Japan?
- How to initiate IITs at an early stage in Japan
- Summary
Why have IITs at an early stage not been conducted in Japan?
Reasons for few IITs in Japan at an early stage

- Western academic groups are more “easy to access” due to geographical reasons and their experience/expertise
- Japan affiliates of global companies prefer to conduct IITs after approval
  - Company is afraid of "getting out of control", for example, leading to more AEs
- There is no unique reason/rationale for global companies to collaborate specifically with Japanese sites
  - Less experience/expertise in IITs under GCP-equivalent conditions
  - Less trust in enrollment
- First step -

To establish operational system to conduct IITs (no support from the company)

- Data management (speed and quality)
- Data analysis, study report
- SAE reporting (pharmacovigilance)
- Drug supply management
- Enrollment system (speed and quality)
- Monitoring
- Insurance coverage
- **Under GCP-equivalent conditions (quality assurance)**
- **Safety and efficacy criteria (CTCAE, RECIST, etc.)**
- **Project management**
What is the second step?

What kind of IITs are being conducted at an early stage in Western countries?
IITs at an early stage (1)

- Company Study
- IIT
- Comb Ph1
  - Comb Ph2
  - Registration Study
- FIH study
  - POM
- POC Major CA
  - Registration Study
- POC Major CA
  - Registration Study
- POC Niche CA
  - Registration Niche CA
  - Approval
    - Fast to market
  - Registration Study
- Approval
- POC Others
- Investigator-Initiated Research (non-clinical)
  - Back Up Plan
  - Registration Study
  - Approval
IITs at an early stage (2)

• **Example 1: generation of fast-to-market plan**
  – A site or research group proposes IITs in a niche indication based on their expertise in that area

• **Example 2: generation of back-up plan**
  – A site proposes and conducts preclinical studies to create new scientific evidence for additional indications and also proposes IITs based on their data

• **In general**
  – Competition is high; only few sites can get an IIT agreement from global companies
  – FIH study sites have more advantages because they already have experiences with new drugs.
- Second step -

- Conduct **preclinical pharmacology studies using unapproved drugs to generate new scientific rationale**
- Have area of specialty with strong expertise
  - **Expertise from preclinical to clinical**
  - Enrollment in appropriate period even if niche cancer
- **Join company-sponsored FIH or early stage studies**
- **Consider the following items**
  - Biomarker analysis
  - Imaging central review (virtual imaging bank for IIT)

→ Important thing is interpretation of the result of POC IIT with small sample size
What is the third step, i.e. more advanced strategy?

What kind of collaborations are conducted from preclinical stage between academia and global companies in Western countries?
Current biomarker-driven early clinical development

Preclinical

Phase I

Conventional way

Phase II

Phases

Phase III

Approval

Translational research

Development of accurate model

Biomarker investigation

Molecular Profiling

Biomarker-driven development

Biomarker validation

POC IIT

Anti-Cancer Symposium Poster Nov 18, 2011
Possible collaboration in early stage development (1)

Sponsor will seek collaborators who have the following expertise:

• Preclinical pharmacology studies
  – Unique animal models expressing target genes/proteins

• Biomarker Investigation
  – Biomarkers related to target genes/proteins, its new technology

• Molecular Profiling
  – Tumor tissue banking and/or measurement of gene/expression rates

• IITs for additional indications
  – Interested in our new drugs and can afford to conduct IITs in additional indications as a back-up plan
Activities in early stage development (3)

Global company
FIH sites, experienced sites, and reliable sites are usually selected as collaborators

Japan affiliates
- Not fully aware of project status at an early stage
- Not usually a member of early stage projects
- Do not make enough efforts to arrange collaborations with Japanese sites

Japan academic sites
- Few sites are interested in both preclinical and clinical development
- Not enough budget/resource to collaborate with global companies at an early stage
- Few groups conducts comprehensive research including translational, biomarker and clinical (IIT)
Team research

- Site A: Basic scientist
- Site B: TR scientist
- Site C: Clinical scientist
- Site D: Biomarker scientist (or venture companies)
- Site C: Statistician
- Site B: Information scientist
- Across site: PM

Support infrastructure

- Japan affiliate
- IITs
- Biomarker study
- Tumor bank
- In vitro in vivo study

Government
- Third step -

• **Japanese sites/groups**
  – Start ‘Team Research’ for comprehensive research including translational, biomarker and clinical (IIT)

• **Japanese affiliates**
  – Get involved more deeply in the program from preclinical stage
  – Interact with Japanese sites/groups (including venture companies) more proactively from preclinical stage

• **Japanese government**
  – Support academia by funding/budgeting not only research work but also establishment of infrastructure for team research
Summary

First step
• Establish operational system for IIT

Second step
• Have area of specialty with strong expertise in basic, translational and clinical (IIT)
• Include biomarker analysis and imaging central review in IIT

Third step
• Japanese affiliates
  – Get involved more proactively from preclinical stage and interact with Japanese sites/groups
• Japanese sites/groups
  – Conduct ‘Team Research’ for comprehensive research including translational, biomarker and clinical (IIT)
• Japanese government
  – Support academia by funding/budgeting team research
Thank you for your attention！
ご静聴ありがとうございました。