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

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- 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

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What is the second step?

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

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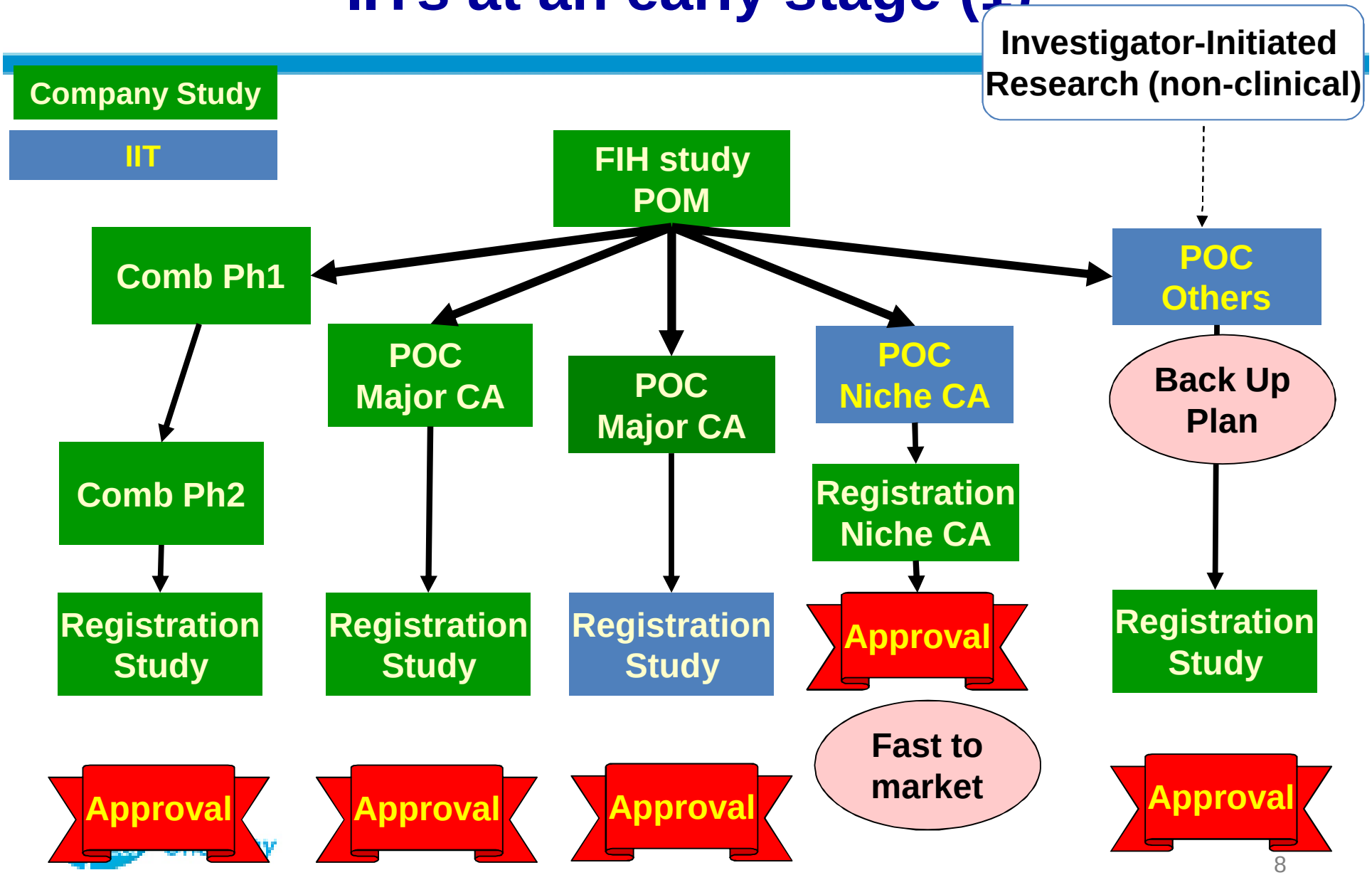
IITs at an early stage (1)



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.**

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- 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**

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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?

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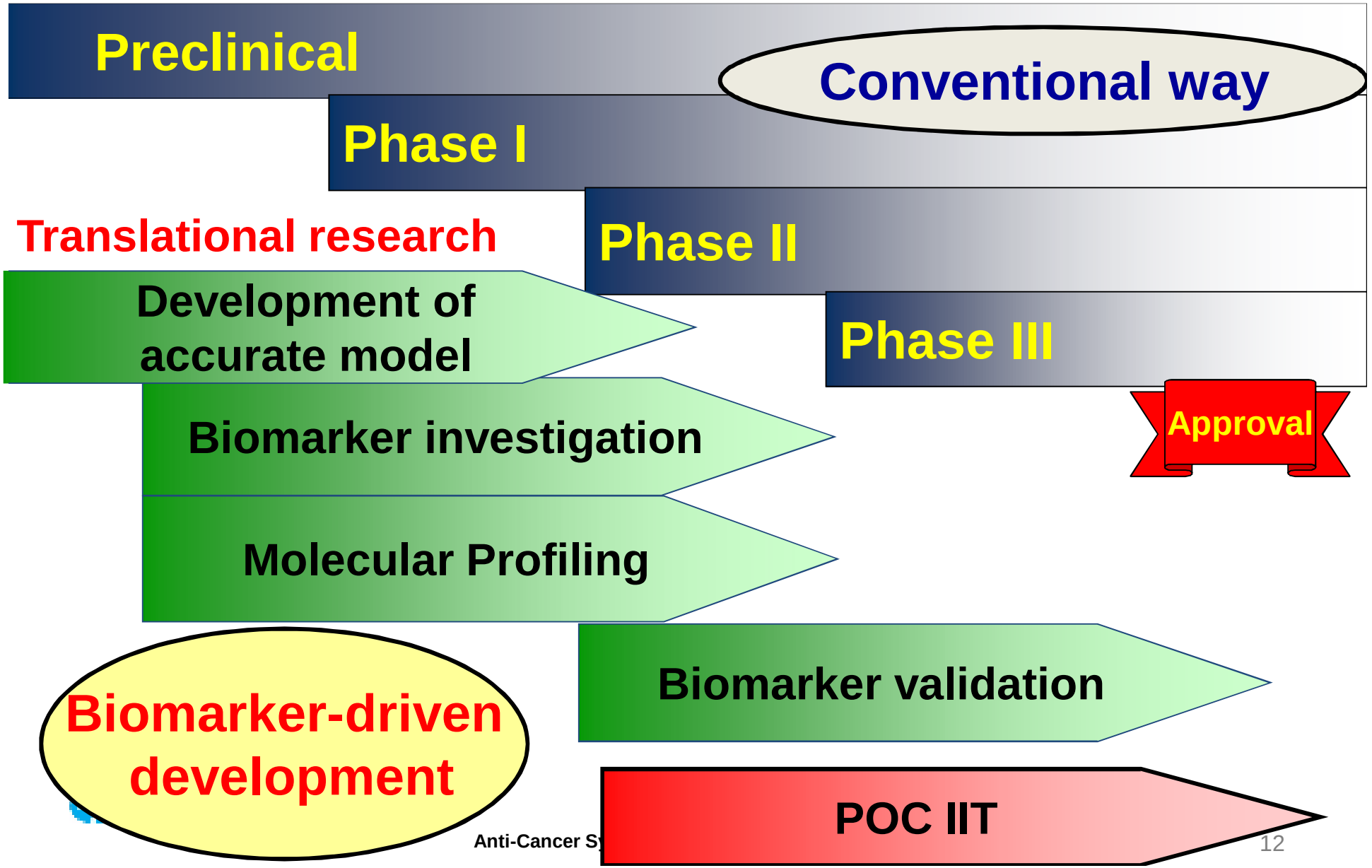
Current biomarker-driven early clinical development



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

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Activities in early stage development (3)

Global company

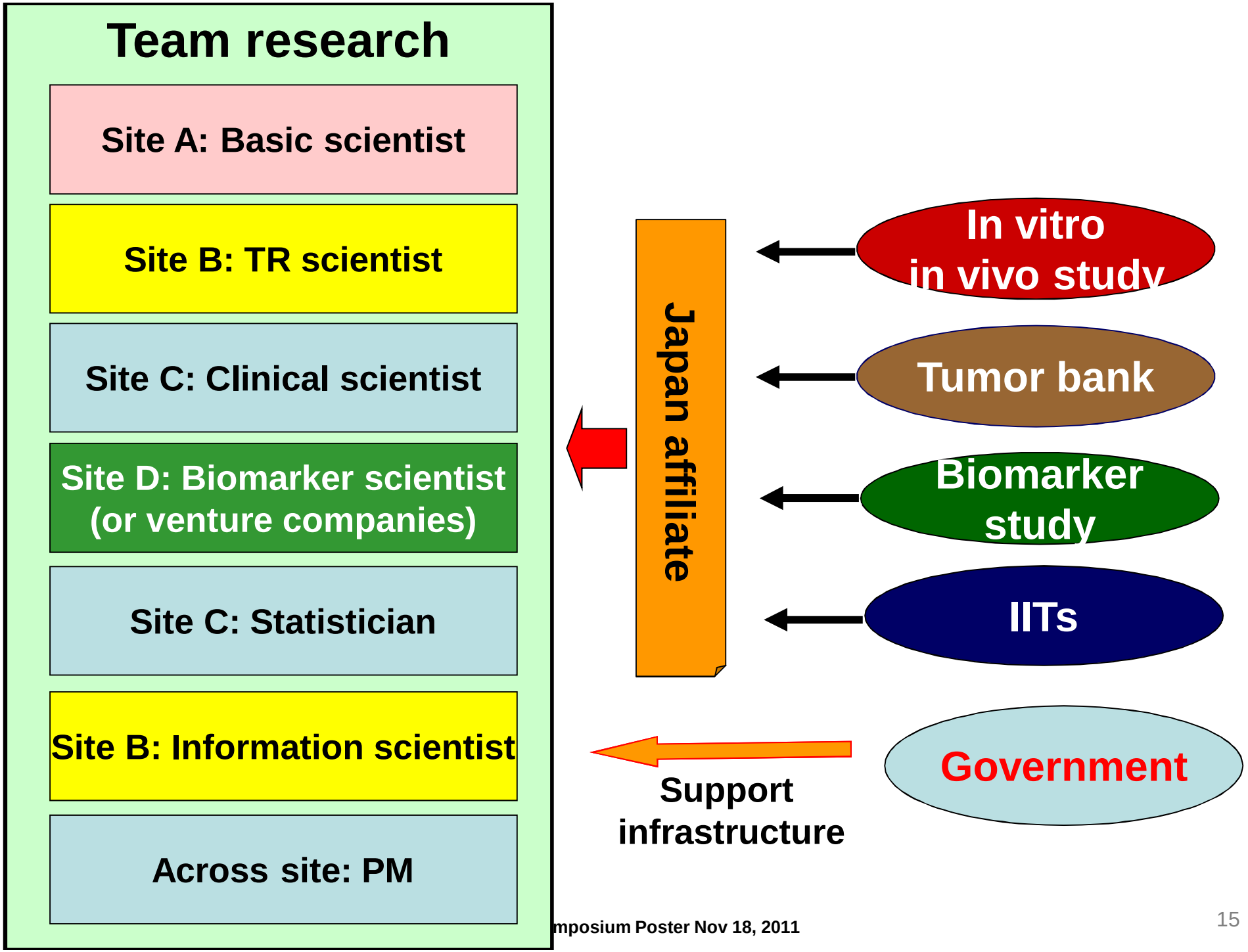
FIH sites, experienced sites, and reliable sites are usually selected as collaborators

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
Japan affiliate
In vitro in vivo study
Tumor bank
Biomarker study
IITs
Government
Support infrastructure

- 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

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Thank you for your attention！

ご静聴ありがとうございました。