Early Global Development from Sponsor's Point of View

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Objective

To discuss points to consider for Japan to join G-FIH (Global First-In-Human) study with Western countries, which will be a base for future global Ph2 and Ph 3 development plans

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Agenda

- Strength and Weakness of Japan
- Eligible Study Site for FIH Study
  - Performance
  - Ability of study sites
  - Ability of investigators/staff
  - Extra values
    - Non-clinical work
    - Investigator Initiated Trials (IITs)
- Regulatory Challenges
- Summary

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Strength of Japan

The number of published articles indicate strength in certain DAs[1)]

Disease Areas	Japan	China	Korea	India	US
Oncology	62	6	4	1	1,446
A&R (Allergy & Respiratory)	13	3	1	0	233
Neurology	75	12	5	1	1,185
Pain	2	0	1	0	54
CVMED	484	60	28	7	6,535
Inflammation	22	3	1	0	339
Immunology	79	9	4	2	1,247
Vaccine	25	11	2	1	575

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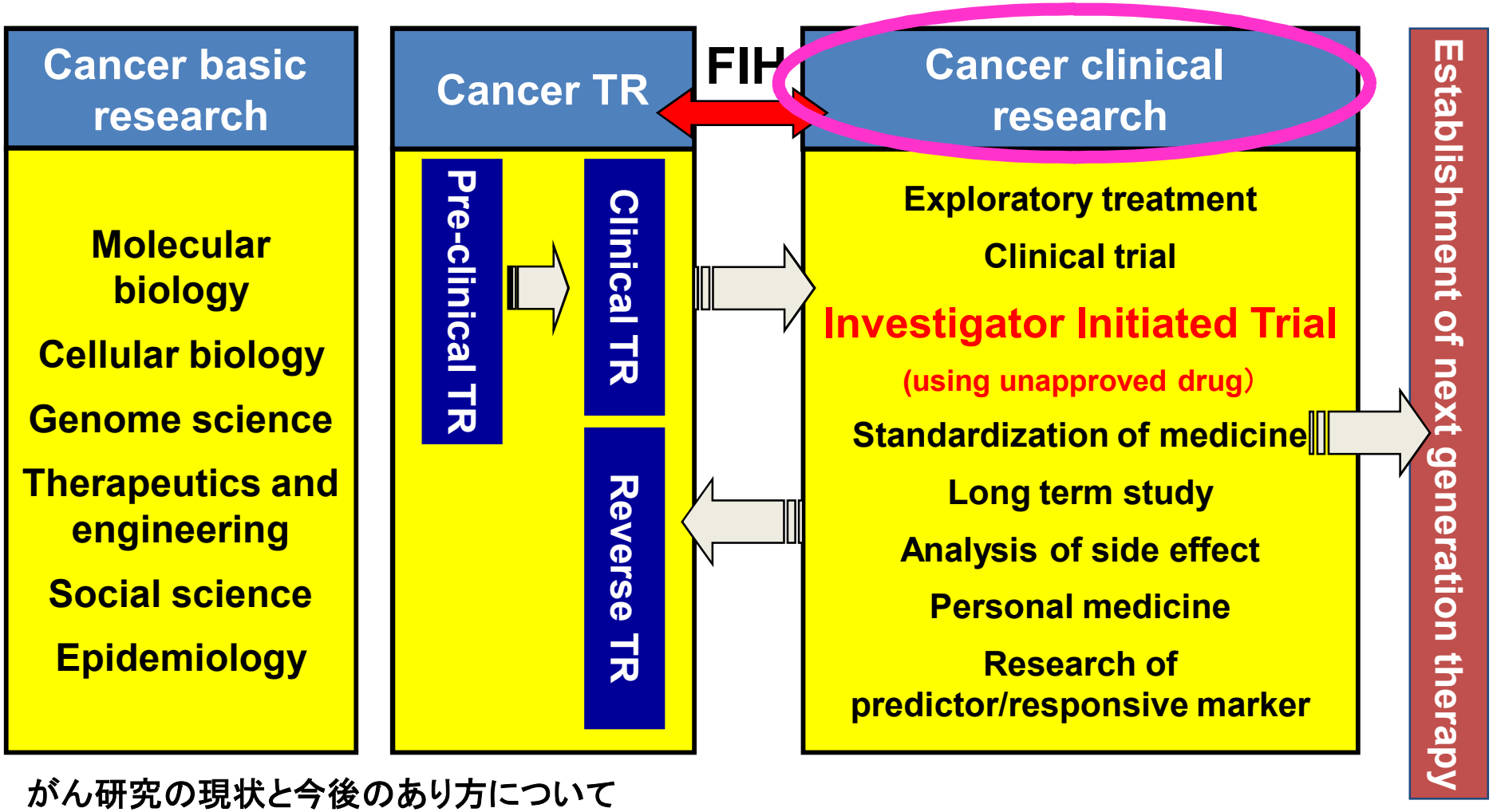
1. Papers published in either Nature or Science
Cumulated results from 2005 to 2010 (as of Nov 18, 2010)

Many Japanese researchers are collaborating with global researchers

Japan is a key global player in basic research

Weakness of Japan



がん研究の現状と今後のあり方について
（平成22年6月25,ライフサイエンス委員会,がん研究戦略作業部会）改変

Lack of experience in G-FIH study and IITs, coming from / resulting in few TR activities

Japan is not yet a key global player in TR and clinical research

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Eligible Study Site for FIH Study (1)

- **Performance**
  - Enrollment speed in various tumor types
    - Constant enrollment throughout the study period
  - CRF data entry (especially AE)
- Ability of study sites
  - Handling unexpected AEs (dermatology, cardiology etc)
  - Imaging technology, tissue sampling etc.
  - Acceptance of innovative/flexible study design
- Ability of investigators/staff
  - Deep discussion with W-investigators in English
  - In depth knowledge of target molecule

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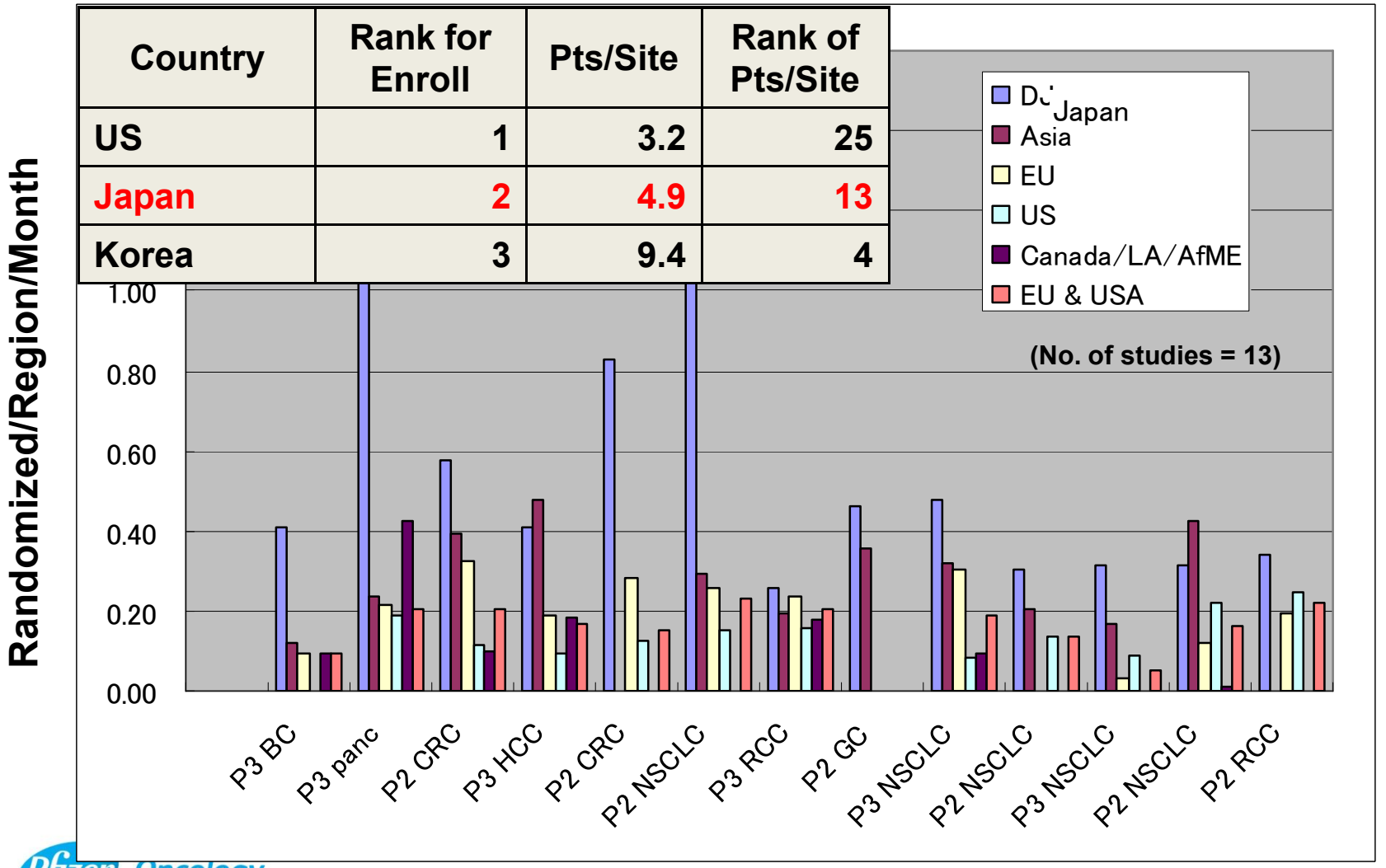
Enrollment Speed

-Number of Patients/site in Global Studies-

Country	Rank for Enroll	Pts/Site	Rank of Pts/Site
US	1	3.2	25
Japan	2	4.9	13
Korea	3	9.4	4



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Source: Pfizer Japan data

Enrollment in Japan is competitive in Ph2/3

For FIH study…
Can we enroll various types of tumors?
Can we constantly enroll patients throughout the study period?

Establish a network with affiliate sites

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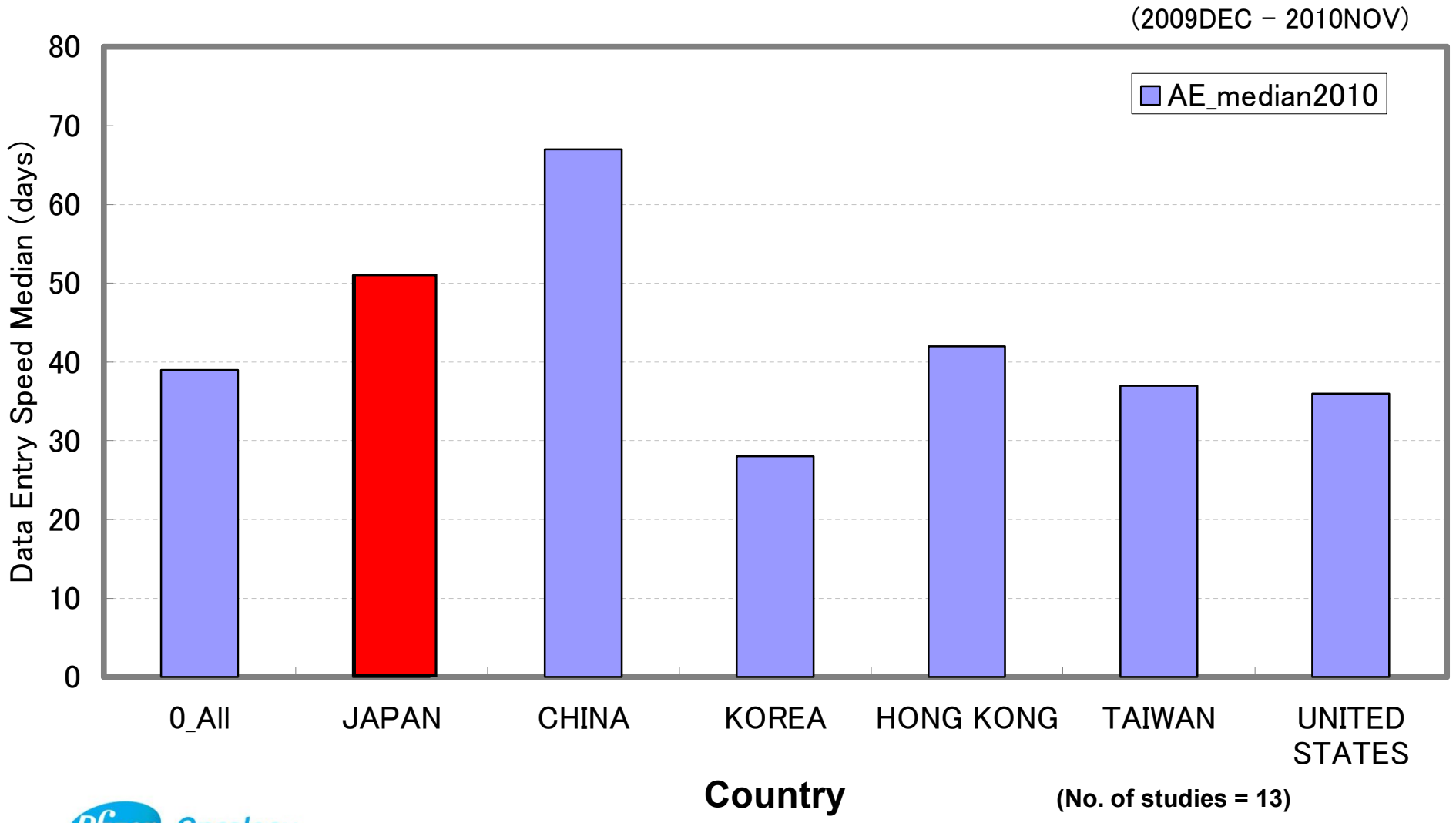
Speed of Data Entry: AE Module
-Median Number of Days in Global Studies-



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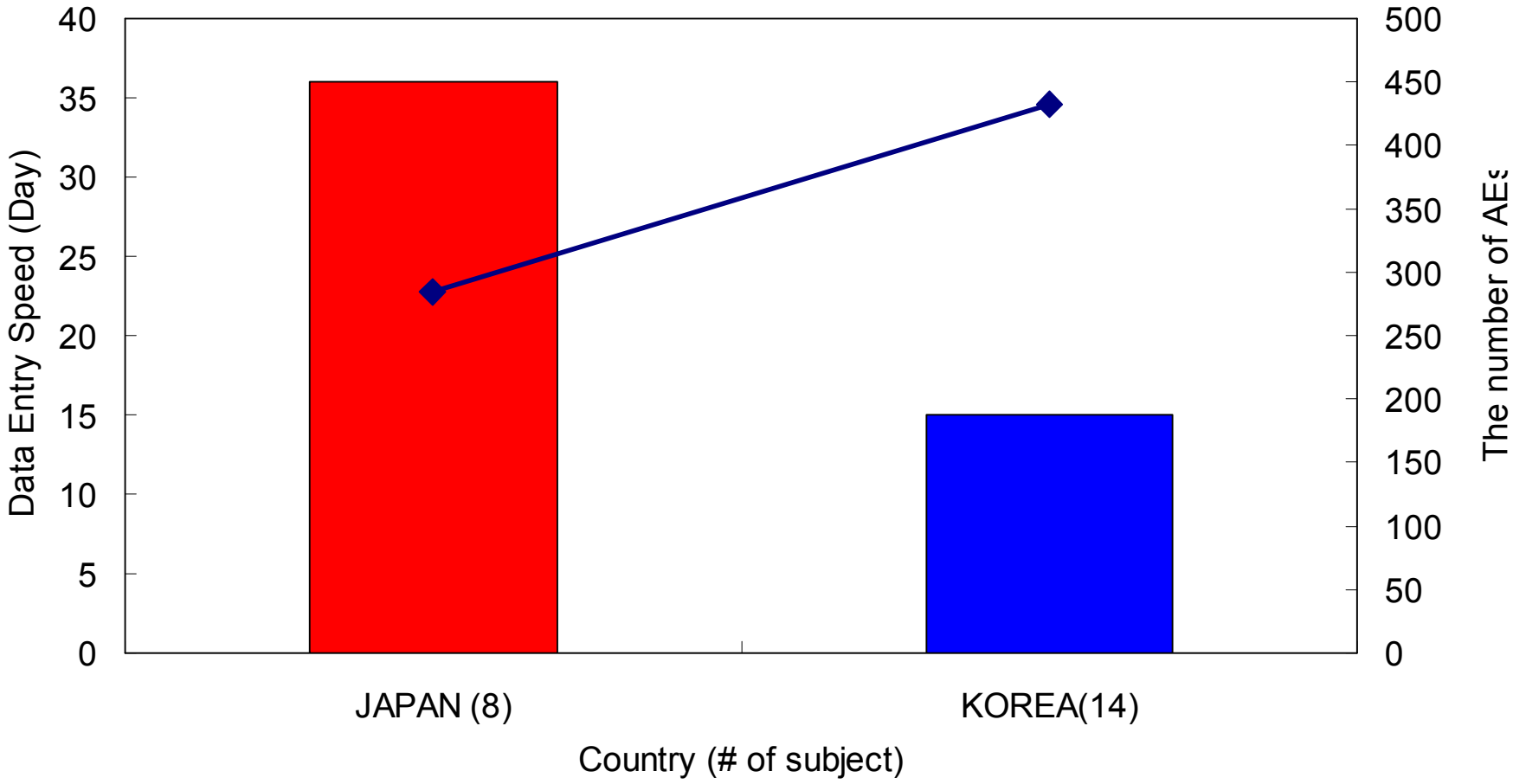
Source: Pfizer Japan data

Speed of Data Entry: AE Module

-Median Number of Days and Number of AEs in a Global Ph1-



(No. of studies = 1)

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Source: Pfizer Japan data

Why Prompt Data Entry is Important?

ALCOA Standard

- Accurate　正確であること
- Legible　判読可能であること
- **Contemporaneous　同時であること**
- Original　オリジナルであること
- Attributable　属性を持つこと，起因性（誰が記載したか、audit trail）

http://www.fda.gov/OHRMS/DOCKETS/98fr/04d-0440-gdl0002.PDF

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Data entry, record, and update must happen at same time.
Data should be recorded once it is generated in order to maintain high quality.

Eligible Study Site for FIH study (2)

- Performance
  - Enrollment speed in various tumor types
    - Constant enrollment throughout study period
  - CRF data entry (especially AE)
- **Ability of study sites**
  - **Handling of unexpected AEs (dermatology, cardiology etc**
  - **Imaging technology, tissue sampling etc.**
  - **Acceptance of innovative/flexible study design**
- **Ability of investigators/staff**
  - **Deep discussion with W-investigators in English**
  - **In depth knowledge of target molecule**

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If these eligibility criteria are met,
Japan can become a player in global studies

Sites with extra values are selected

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Extra Values: Proactive research

- **Proactive involvement in optional tumor sampling and diagnosis assessment (IHC, gene expression profile, etc)**
- **Conduct of additional non-clinical pharmacology studies for other potential indications and/or treatment concepts**

Extra Values: Proactive Research
- Proposal-

Establish collaborations among clinical site, non–clinical Sites, and Sponsor

Clinical study sites

TR

Science from Japan/Asia

Sponsor

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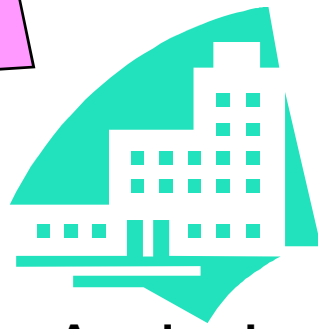
TR



Academia
Basic research sites
(non-clinical site)

Extra Values: Investigator Initiated Trials (IITs)

- **Overseas, IITs are conducted after FIH or POM**
- **In Japan, examples of IITs using new agents are limited**
  - **Difficult to get an agreement on IITs from global company**
    - **Hard for global company (HQ) to understand Japan insurance system and clinical research system**
  - **Little knowledge of study sites capable of conducting IITs with new agents under ICH-GCP**

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- ***Study sites should establish a system for IITs***
- ***PMDA/MHLW and sites should appeal their ability/acceptability of conducting IITs***

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Regulatory Challenges

Current situation

- Few examples of G-FIH study with Western countries in Japan due to concern on ethnic differences
  - Korea can Join G-FIH study with any country
- Data on recommended dose in Japanese is required
    - Concern on safety in Japanese population
- Separate J-IND/ Protocol is required when core protocol elements are amended
    - Study objective, design, target population, etc. are frequently modified based on emerging clinical data

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Sponsor, study sites, and PMDA should work together for Japan to join G-FIH study

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Summary

- **Strength and weakness of Japan**
  - *Japan is a key global player in basic research, but not yet in TR and clinical research*
- **Eligible study site for FIH study**
  - *Improvement in performance and ability of study sites/investigators/staff is required to be selected for FIH study site*
- **Extra values such as non-clinical work and IITs**
  - *Proactive involvement in optional tumor sampling and diagnosis assessment (IHC, gene expression profile, etc)*
  - *Conduct of additional non-clinical pharmacology studies for other potential indications and/or treatment concepts*
  - *Investigator Initiated Trials*
- **Regulatory challenges**
  - *Sponsor, study sites, and PMDA should work together for Japan to join G-FIH study*

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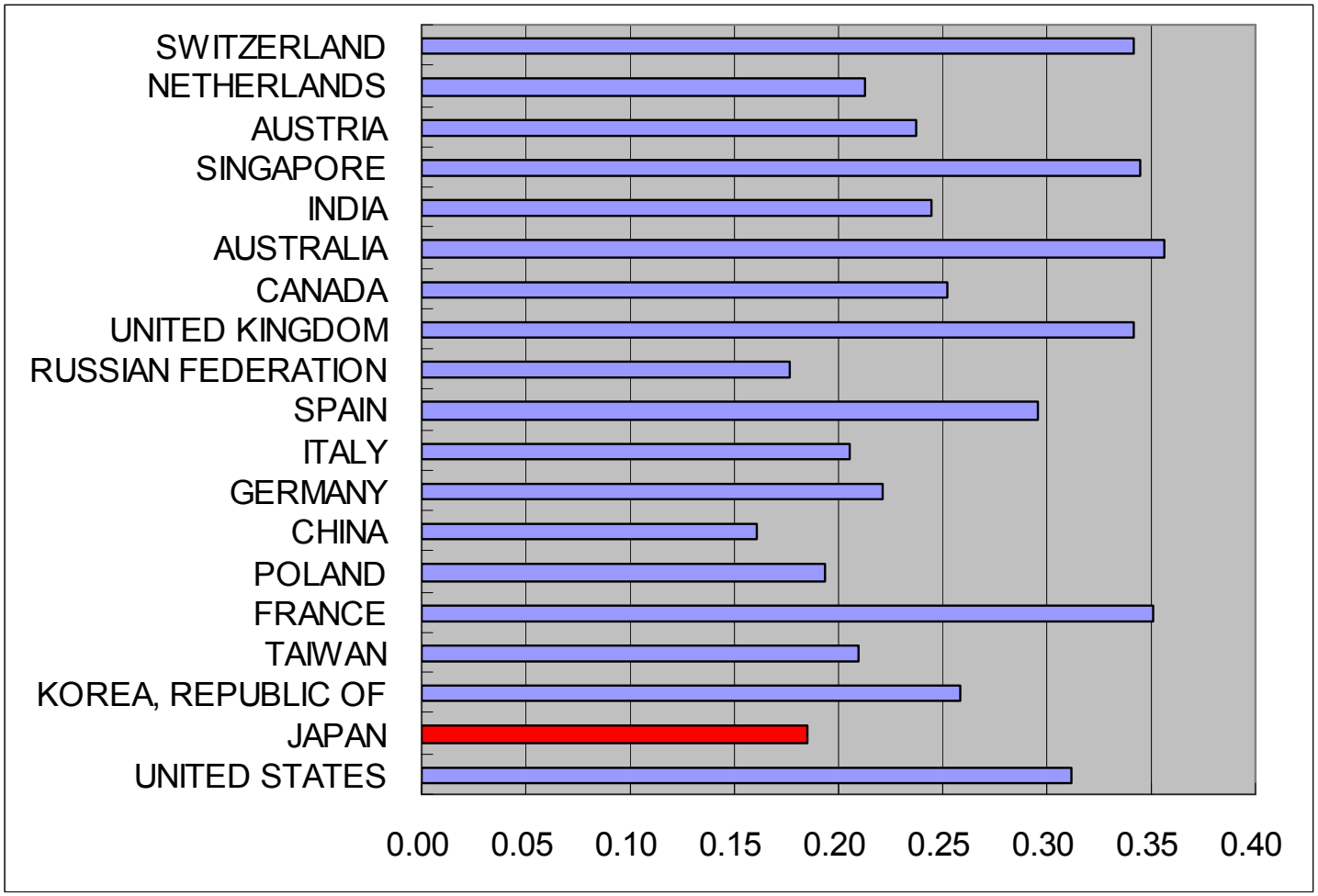
Thank you for your attention！

ご静聴ありがとうございました。

Quality of Data Entry
-Number of Queries in Global Studies-



(No. of studies = 13)

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Source: Pfizer Japan data

Improvement in Perception of Clinical Trials

- **Education of patients**
  - Understand difference between research and treatment
  - Balanced expectation on efficacy and safety
    - In some cases, single agents may not show efficacy
- **Fair message on clinical research from media**