アジアにおける開発体制
-企業の立場から-

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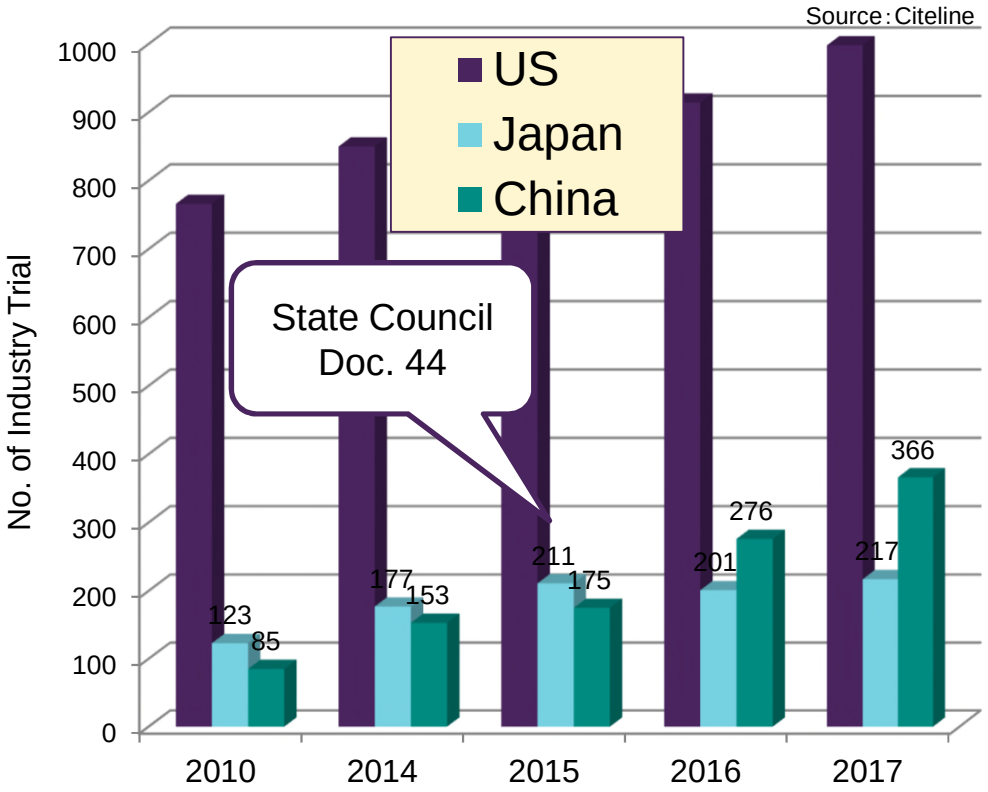
Background

- **Recently clinical development in China is dramatically growing**



- **Chinese Government initiates significant regulatory reforms as “ The Innovation Opinion” containing 36 specific revisions**

(State Council Doc. No42)

- *Reforming clinical trial management*
- *Accelerating drug device review and approval process*
- *Balancing development of innovative drugs and generic drugs*
- *Life-cycle management of drugs and devices*
- *Enhancing drug and medical device review and enforcement force*
- *Implementation of the innovation opinion and coordination among the relevant administrative agencies*

- **In addition, basic research and translational research are also advancing in other Asian countries such as China**
  - China’s 2016-2020 5-year plan prioritizes bio R&D as a key focus area; 2016 allocated 30% of social development budget (Justin C et.al. NEJM. 2014)
- **Now is the time to think again about Japan’s position in drug development and where should we head**

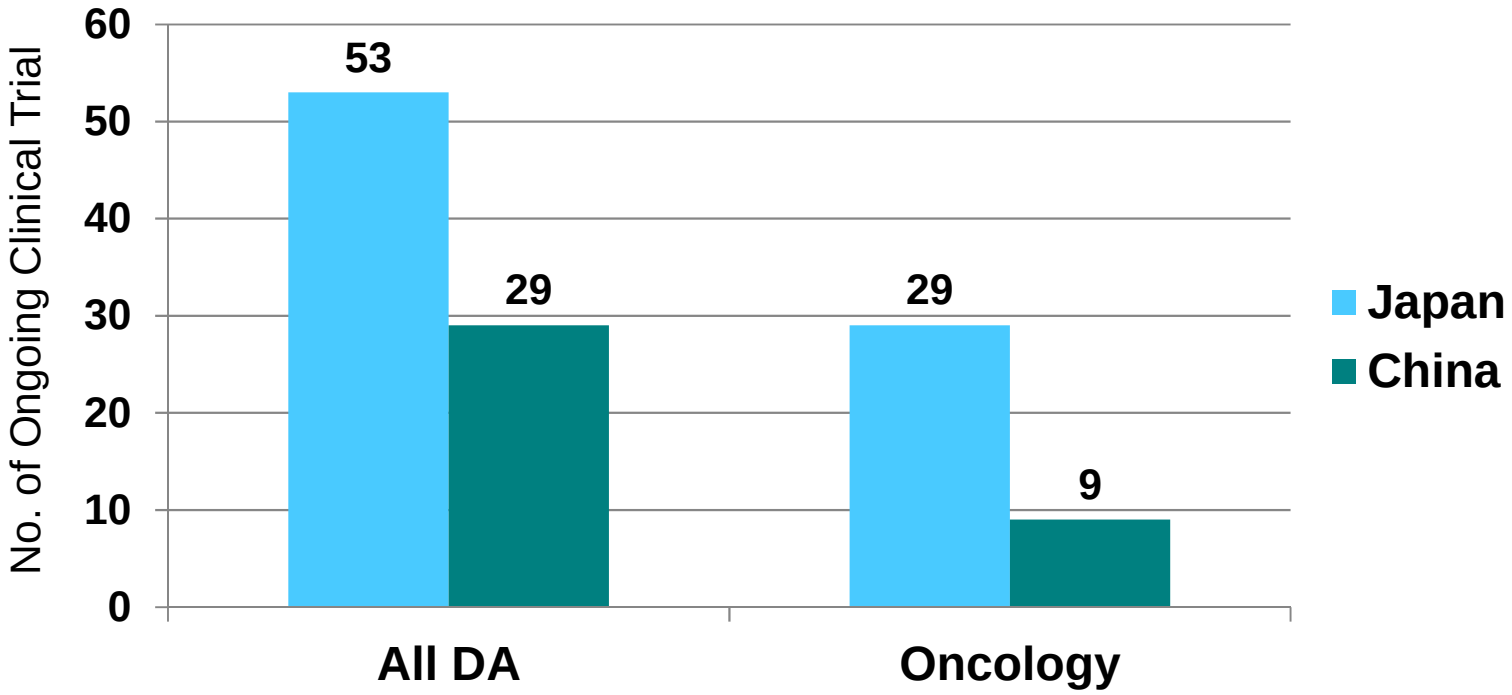
Clinical Research

Basic and Translational Research

Clinical Research

Clinical Research: Organization and Number of Trials

- **~340 members in Dev-Japan vs 160 members in Dev-China (excluding direct global lines)**
- **Clinical: 50 members in Japan vs 24 members in China**



Japan has great advantages over China so far;
China has been struggling to participate into global studies

Japan has a great advantages over China " So Far"

<Advantage>:"Matured"

- **Regulatory advantage**
  - **Necessity of Phase 1 before registration trial**
- **Well-organized Japan affiliate (Established reliance from global)**
  - **Studies led by Pfizer Japan had "fastest record" among Project A (project buy-up to protocol finalization and FSFV)**
- **Sufficient capability at study sites**
  - **Sufficient experience, including Phase 1 (DLT evaluation etc)**
  - **Speedy start up and commitment (contribution to short cycle time)**
  - **GCP compliance and quality**
- **Strong leadership of Japan KOLs in certain areas**

<Disadvantage>: "COSTLY"

- **Highest cost for FTE (both internal and CRO cost)**
- **Less performance per CRA/site than other Asian countries**
- **Post marketing requirement (PMS, all case survey etc)**
- **Regional Specific/Strict requirement for IVD and CDx**

China has been struggling to participate in global studies

CFDI:Center for Food and Drug Inspections
ACLOA: Attributable, Legible, Contemporaneous, Original and Accurate
CCEA: Complete, Consistent, Enduring and Available

<Advantage>

- **Huge potential of enrollment**
- **Performance per a CRA/site is high**
- **Participation into global registration study using Japanese PK & safety data**

<Disadvantage>

- **Slow study start up**

⇨ ***One of the KEY focus area of " The Innovation Opinion" is "Reforming clinical trial management" , which could substantially reduce delays in the approval of clinical trial applications*** (Nov 6th, 2017: www.cov.com)

- **Quality issues (Field inspection detected 28.1% did not meet ALCOA+CCRA)**

⇨ ***Intensive training for CRA is requested by the CFDI***
The CFDI is expanding and hiring more staff, and the training is more standardized and consistent **(J Evid Based Med. 2018; 11:3-6)**

- **Less experiences of Phase 1 (DLT evaluation)**
- **Biospecimen assay (difficulty to implement companion diagnostics)**

⇨ **Global accepts "Dare To Try" for CHINA**

Now most pharma have strong interest in China

Made the call! China Regulation Reform (SC No. 44/42)

- **Modernization and standardization to global norms of regulation**
- **Has shifted from emerging market to innovative drug/health**
  - **Japan is now strengthening use of generics in priority prefectures**
- **Implemented "conditional approval" for innovative drugs**

  48 products selected as " Fast Track"

  Palbociclib was approved in Aug 2018 with 2 years acceleration based on Chinese PK study only
- **(Will?) improve medical device regulations and harmonize them with international practices**

⇨ **Global organization proactively includes China into ongoing/future global registration studies!**

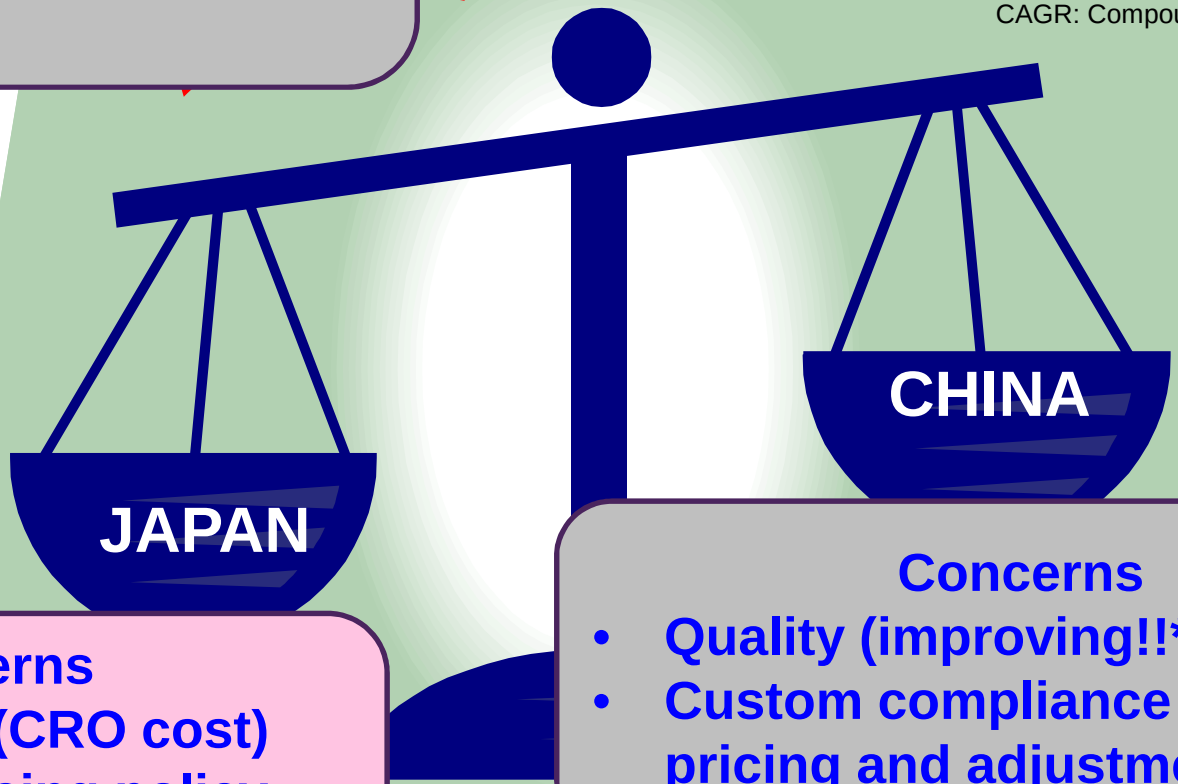
1) http://www.ey.com/Publication/vwLUAssets/ey-life-sciences-report-asia-march-2017/$FILE/ey-life-sciences-report-asia-march-2017.pdf

Considerations

Advantages
- Speed of SSU
- Plenty of successful experiences in clinical trials (both internal and external)

Advantages
- Highest CAGR
- Huge potential of accrual
- Changing regulatory environments
- Big data
- Digital health

CAGR: Compound average growth rate



Concerns
- Highest FTE (CRO cost)
- New drug pricing policy
- All case survey
- PMS

Concerns
- Quality (improving!!*)
- Custom compliance (import pricing and adjustment)

*J Evid Based Med. 2018; 11:3-6

What should we do??

In China, simultaneous development/submission/approval would become standard like current Japan

Japan needs *more cost efficient study management* as a first step

- **More disruptive idea using IT, digital platform etc**
  - **Risk Based Monitoring**
  - **eSource, eICD etc..**
  - **More efficient PMS and all case survey to reduce overall cost of drug development**
- **More "patients centric approach"**

As a next step, Japanese must become global players in global organization, not considering only Japan but also the globe

It is a high time
to be a real global role from a region

Basic and Translational Research Partnering with Academia

Basic/Translational Research Collaboration/Partnering Model

PI: Principle investigator

- One on One Collaboration
- CTI (Center for Therapeutic Innovation), "a Joint Project"
  - Collaboration through the research center consisted of several academia and Pfizer to conduct drug R&D (from the stage of idea creation to a first in human study)
- ITEN (Innovative Target Exploration Network)
  - Partnering model with selected academic institutions and PIs for early-stage "research project" that have the potential to deliver innovative therapeutic targets

Collaboration with multiple institutions/researchers become one of standard partnering models.
Global is now very interested in collaboration with Asian countries.

Summary

- **Number of clinical trials in Japan is still higher than China**
- **However, huge investment to China has been committed due to highest CAGR, high potential of accrual, change of regulatory environments etc.**
- **Japan performance is good in study start up and quality, however needs to improve study cost (CRO/CRA cost), performance per CRA/site using innovative IT tools; more patient centric approaches should be promoted proactively**
- **In addition, Japan affiliates need to expand it's role**
  - **Become a global role (more global assignment of Japanese)**
  - **Japan clinical members should be involved in open innovation activities with daily communications not only on clinical but also on basic/translational research topics**