外資系企業における開発品目の傾向
～PhRMA/EFPIA合同調査結果より～

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PhRMA/EFPIAで実施した2019年度の合同調査結果は以下の通りであった。

- 2019年度（2019年4月～2020年3月）にPhRMA及びEFPIA加盟会社で開発中のプロジェクトは661品目、臨床試験は777試験であった。プロジェクトの69%が新有効成分含有医薬品、55%が抗悪性腫瘍薬であり、また臨床試験の82%が国際共同試験であった。
- 米国Breakthroughの指定を目指すプロジェクトは15%であったのに対し日本の先駆け審査指定制度は5%に留まり、その主な理由は日本で最初に申請することを含む指定要件を満たせないことであった。更に米国では早期承認に向けて、効能追加も含め、RTORやOrbis等の制度も活用されていた。
- 小児も対象にしたプロジェクトは21%（小児のみ6%、成人および青年期等15%）で、成人のみを対象とした79%のプロジェクトのうち今後小児開発を計画しているのは9%であった。小児開発促進のハードルは主に試験の実施関連、インセンティブは薬価上のメリット等と回答が得られた。
- ICH E17の利用についても僅かながら対面助言で相談されている状況が分かった。
- 多くの品目で海外と同時開発が進められ、日本先行もしくは同日申請は10%未満だが、約60%の品目で海外から3ヶ月以内の申請（同時申請）を予定していることが示された。
- 80%以上の会社で「日本人データへの拘り」が開発着手ラグ解消の課題と考えていることが示された。
- オーファン指定に関しては、最適と考える相談時期と現状に乖離がみられるなど、改善点が伺われた。

PhRMA-EFPIA Joint Survey 2020

- Clinical Studies and Development Plan
  - Projects ongoing in FY2019
  - Global and local studies ongoing in FY2019
  - Interaction with the agency for global studies

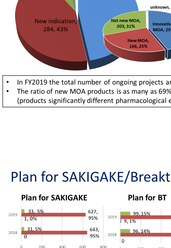
Participating companies:

PhRMA (11 companies)
- Abbvie, Alexion, Amgen, Biogen Japan, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Pfizer, and Gilead Sciences

EFPIA (15 companies)
- AstraZeneca, Bayer, CHUGAI, CSL Behring, Ferring, GlaxoSmithKline, Janssen, LEO, Lundbeck, Merck Biopharma, Boehringer Ingelheim, Novartis, Novo Nordisk, Sanofi, and UCB

Total Projects in FY2019

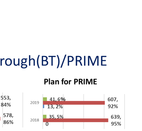
Projects by Planned filing Category



EFPIA + PhRMA 661 projects

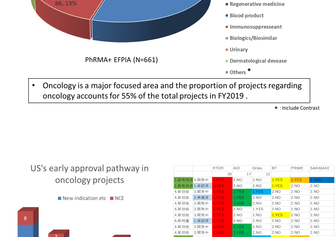
Development Status

In-license product



- In FY2019 the total number of ongoing projects are 661. 87% in total are in-development product.
- The ratio of new MOA products is as many as 69%, of which innovative new MOA products (products significantly different pharmacological effecting compare with existing drugs) are 44%.

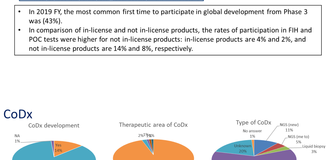
Therapeutic Area for Projects in FY2019



- Oncology is a major focused area and the proportion of projects regarding oncology accounts for 55% of the total projects in FY2019 .

Include Contrast

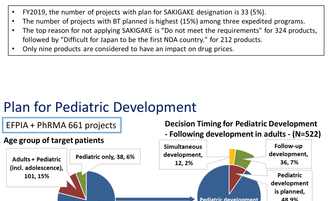
First Time to Participate in global development



Others（Free comment）
- Local development
- In progress local Phase 1/ local study
- Local development due to delay to global development
- Not yet, but willl participate global development in the future

- In 2019 FY, the most common first time to participate in global development from Phase 3 was (43%).
- In comparison of in-license and not in-license products, the rates of participation in FIH and POC tests were higher for not in-license products: in-license products are 4% and 2%, and not in-license products are 14% and 8%, respectively.

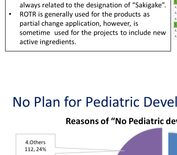
Plan for SAKIGAKE/Breakthrough(BT)/PRIME



Other reasons （Free comment）
- Consultation for Japan has not determined yet
- Under consideration for license-out/ Will be license-out
- No NDA plan
- Halt the development
- Had been designated

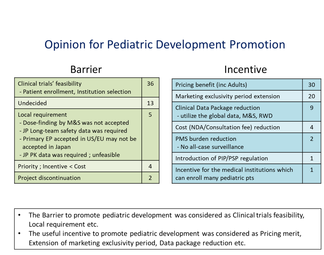
- FY2019, the number of projects with plan for SAKIGAKE designation is 33 (5%).
- The number of projects with BT planned is highest (15%) among three expedited programs.
- The top reason for not applying SAKIGAKE is "Do not meet the requirements" for 324 products, followed by "Difficult for Japan to be the first NDA country." for 212 products.
- Only nine products are considered to have an impact on drug prices.

US's early approval pathway in oncology projects



- There is a trend that the projects to use RTOR (Real time Oncology Review) intend to use Assessment Aid.
- There is a trend that the projects to use RTOR have plan for designation of BT.
- The designation of BT in these projects is not always related to the designation of "Sakigake".
- RORTR is generally used for the products as partial change application, however, is sometime used for the projects to include new active ingredients.

CoDx

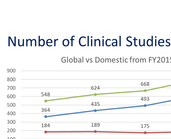


- 95% of CoDx development was accompanied with cancer drug development.
- NGS and liquid biopsy were found in addition to general CoDx development.
- In accordance with change of regulation, some companies investigate whether or not CoDx development is included as the target of categorization of drug development.

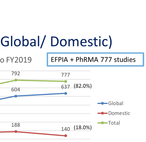
Plan for Pediatric Development

EFPIA + PhRMA 661 projects

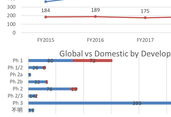
Age group of target patients



Decision Timing for Pediatric Development ＊Following development in adults - (N=522)



MRCT (included in PIP/PSP) participation plan? (N=48)

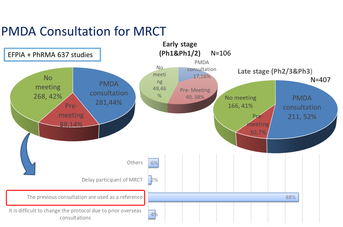


PMDA consultation plan for CCDP?
Yes 19%
No 81%

- 21% of all projects were developed in pediatric patients.
- As for the projects developed only for adults patients, 9% (48cases) was planning pediatric development, and its decision timing was the same as overseas. Its 75% (36 out of 48cases) was follow-up development.
- For pediatric development, about 70% projects expected to participate in the MRCT (PIP/PSP), and 19% of them had PMDA consultation plan for CCDP.

No Plan for Pediatric Development

Reasons of "No Pediatric development plan" (N=473)



Other reasons

Undecided	78
Diseases specific to adults	25
Project discontinuation	5

- The reason for not planning of pediatric development was No plan globally (314 cases, 66%), Low Priority (45 cases, 10%), J-pts data is to be required (2 cases, 0.4%).
- The reason for not developing even locally was No medical needs (81%) and Low Clinical Trial feasibility (14%).

Opinion for Pediatric Development Promotion

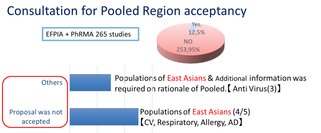
Barrier		Incentive	
Clinical trials' feasibility - Patient enrollment, Institution selection	36	Pricing benefit (inc Adults)	30
Undecided	13	Marketing exclusivity period extension	20
Local requirement - Dose-finding by M&S was not accepted - JP Long-team safety data was required - Primary EP accepted in US/EU may not be accepted in Japan - JP PK data was required ; unfeasible	5	Clinical Data Package reduction - utilize the global data, M&S, RWD	9
		Cost (NDA/Consultation fee) reduction	4
		PMS burden reduction - No all-case surveillance	2
		Introduction of PIP/PSP regulation	1
Priority ; Incentive < Cost	4	Incentive for the medical institutions which can enroll many pediatric pts	1
Project discontinuation	2		

- The Barrier to promote pediatric development was considered as Clinical trials feasibility, Local requirement etc.
- The useful incentive to promote pediatric development was considered as Pricing merit, Extension of marketing exclusivity period, Data package reduction etc.

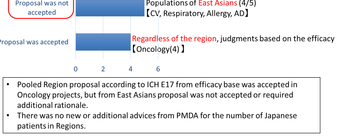
Number of Clinical Studies (Global/ Domestic)

EFPIA + PhRMA 777 studies

Global vs Domestic from FY2015 to FY2019

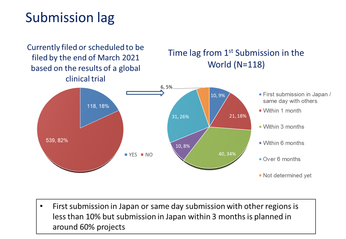


Global vs Domestic by Development Phase



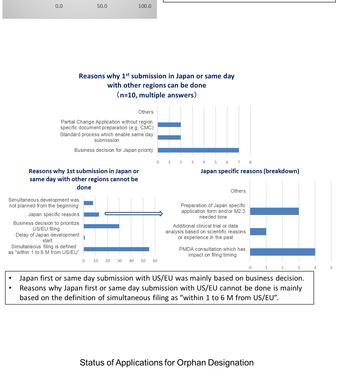
- The total number of studies was 777 and the ratio of Global studies was 82% in FY2019.

PMDA Consultation for MRCT



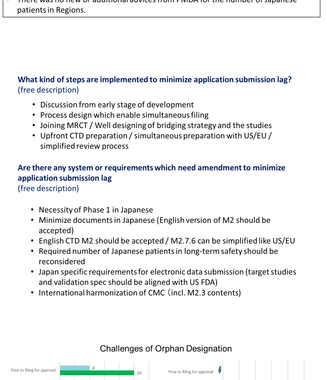
- PMDA meeting were held before starting MRCT at the rate of 58%. The main reason why no PMDA meeting is that the previous consultation are used as a reference.

PMDA Consultation for JP Long-term safety



- The main reasons for no consultation as others were "Early stage of development " or " Small number of patients" .
- The number of Japanese patients of long-term safety included foreign data, or 100 or less Japanese sample size was accepted in approx. half.

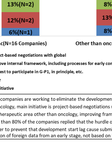
Consultation for Pooled Region acceptancy



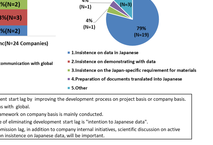
- Pooled Region proposal according to ICH E17 from efficacy base was accepted in Oncology projects, but from East Asians proposal was not accepted or required additional rationale.
- There was no new or additional advices from PMDA for the number of Japanese patients in Regions.

Submission lag

Currently filed or scheduled to be filed by the end of March 2021 based on the results of a global clinical trial

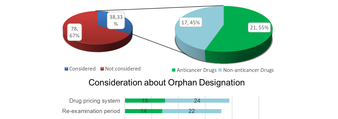


Time lag from 1st Submission in the World (N=118)

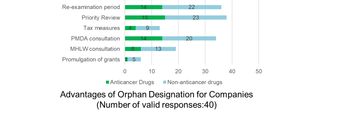


- First submission in Japan or same day submission with other regions is less than 10% but submission in Japan within 3 months is planned in around 60% projects

Reasons why 1st submission in Japan or same day with other regions can be done



Reasons why 1st submission in Japan or same day with other regions cannot be done



- Japan first or same day submission with US/EU was mainly based on business decision.
- Reasons why Japan first or same day submission with US/EU cannot be done is mainly based on the definition of simultaneous filing as "within 1 to 6 M from US/EU".

What kind of steps are implemented to minimize application submission lag?

(free description)

- Discussion from early stage of development
- Process design which enable simultaneous filing
- Joining MRCT / Well designing of bridging strategy and the studies
- Upfront CTD preparation / simultaneous preparation with US/EU / simplified review process

Are there any system or requirements which need amendment to minimize application submission lag

(free description)

- Necessity of Phase 1 in Japanese
- Minimize documents in Japanese (English version of M2 should be accepted)
- English CTD M2 should be accepted / M2.7.6 can be simplified like US/EU
- Required number of Japanese patients in long-term safety should be reconsidered
- Japan specific requirements for electronic data submission (target studies and validation spec should be aligned with US FDA)
- International harmonization of CMC（incl. M2.3 contents)

Internal initiatives to resolve the development start lag

- Many companies are working to eliminate the development start lag by improving the development process on project basis or company basis.
- For oncology, main initiative is project-based negotiations with global.
- For therapeutic area other than oncology, improving framework on company basis is mainly conducted.
- More than 80% of the companies replied that the hurdle of eliminating development start lag is "Intention to Japanese data".
- In order to prevent that development start lag cause submission lag, in addition to company internal initiatives, scientific discussion on active utilization of foreign data from an early stage, not based on insistence on Japanese data, will be important.

Status of Applications for Orphan Designation

Consideration about Orphan Designation

Advantages of Orphan Designation for Companies (Number of valid responses:40)

Challenges of Orphan Designation

Timing of Consultation Regarding Orphan Designation

Suitable Timing of Consultation Regarding Orphan Designation

Key findings：
Approximately 40% of drugs of which application forms have been or are scheduled to be filed are under consideration about orphan designation(Anticancer drugs account for approx. 55%).
There are some advantages of orphan designation for companies regarding drug pricing, re-examination period, priority review, preferential consultation, and etc. On the other hand, the best timing of consultation doesn't match the reality, and there are many demands for making decision based on early data.

Problems with Orphan designation