

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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【主な調査項目】開発品目の状況、日米欧の迅速制度指定状況、RWDの活用、小児・特定用途医薬品開発状況、ICHE17の活用(併合地域戦略)、国際共同治験におけるPhase1試験実施状況、申請ラグ、中国における開発状況 【調査対象企業】 PhRMA(11社):Abbvie, Amgen, Biogen Japan, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline*, Janssen*, MSD, Pfizer, Gilead Sciences, CSL Behring* EFPIA(15社I):AstraZeneca, Bayer, CHUGAI, CSL Behring*, Ferring, GlaxoSmithKline*, Janssen*, LEO, Lundbeck, Merck Biopharma, Boehringer Ingelheim, Novartis, Novo Nordisk, Sanofi, UCB (*:両団体参加会社,集計は1社として調整済) 【調査結果】 2021年度(2021年4月~2022年3月)にPhRMA及びEFPIA加盟会社で治験実施中の品目は884品目(医薬品 869品目、再生医療等製品 15品目)であり、疾患領域では2020年度に引き続き抗悪性腫瘍薬が最も多く、53%を占めていた。また、全体の48%が新有効 成分であり、全体の62%は新規作用機序であった。 治験の実施数は1043件であり、そのうち861件(82.6%)は国際共同治験であった。 先駆的医薬品指定制度の利用品目数は検討中も含めて全体の2%であり、指定申請しない理由は2020年度と同様、世界で最初の申請を行うことが難しい等の理由が多かった。 欧米における抗悪性腫瘍薬の早期承認制度(RTOR, Assessment Aid, Project Orbis)を利用する品目は、新有効成分では2020年度(それぞれ20、19、20品目、以下同順)と2021年度(20、18、21品目)で変化はみられず、効能追加等の一変では2020年度(9、4、8品 目)から2021年度(26、21、34品目)で増加していた。 小児開発を進めている品目は、全体の19%であり、そのうちの72%は国際共同治験によるものであった。 ICH E17に従い、併合地域戦略について対面助言を実施した品目は、相談を行った品目の8件(3%)であり、2020年度の20件(8%)より減少した。 リアルワールドデータ(RWD)の活用を検討している品目は全体の21件(2%)と非常に少なかった。RWDの活用について、当局と相談した結果、活用を予定している品目は7件であり、主な利用目的はプロトコール作成時の根拠としての利用または、申請資料に対する 有効性・安全性の補完であった。 新有効成分のうち、16% (44/273)は日本でPhase1を実施せず国際共同治験に参加/参加予定であった。日本でPhase1を実施予定の品目(132件)のうち、17%(22件)がSafety Run-in Cohortを実施していた。 世界最初の申請から3ヵ月以内で本邦の申請を予定している品目は約59%であり、その割合は昨年(51%)より増加していた。

中国における開発状況について、国際共同治験に参加している品目は36%であり、その多くはPhase3からの参加であった。



- products that are in development
- The ratio of new MOA products is as many as 62%, of which 35% are innovative new MOA products (i.e., products that have a significantly different pharmacological effect compared with existing drugs)

Use of Early Approval Pathway in Oncology Projects









requirements or that it is difficult to submit applications in Japan before or at the same time as the first global application.

Utilization of Real-World Data (2/2)



- Of the 21 projects in Japan and 23 project in the U.S., 7 (CNS:3, Oncology:1, Blood product:1, Regenerative medicine product:2) in Japan and 11 (CNS:4, Oncology:2, Regenerative medicine product:3) in the U.S., RWD will be utilized based on the HA consultation. 6 projects will utilize in both regions.
- Of the 7 projects in Japan, most frequent reason for utilizing RWD was to generate evidence for protocol creation. Of the 11 projects in the U.S., the primary objective was to complement efficacy/safety data in addition to clinical trials.
- The company gave up using RWD in three cases in Japan and one case in the U.S. as a result of the HA consultation, which requested to conduct clinical trial.

Therapeutic Area for Projects in FY2021

Oncology is a major focus area accounting for 53% of the total projects in FY2021.

Utilization of Real-World Data (1/2)

• Of the new active ingredients that participated in MRCTs from P2, 66 projects (75%) conducted J-P1 prior to MRCT participation, which was a higher proportion than for those that participated in MRCTs from P3.

• Among new active ingredients, more projects in in-licensed products participated in MRCTs from P3 (57 (54%)) than whole new active ingredients, and 39% of them conducted J-P1 before participating in MRCTs, which was lower than the proportion of whole new active

ingredients (57%). In addition, a higher proportion of in-licensed products were implementing J-P1 in parallel with MRCTs.



- Most (118 or 72%) of these were being developed globally, of which 52 (44%) included data packages that had been agreed with PMDA
- Reasons for prioritizing include global plan, followed by IP and pricing incentives.
- Other responses indicated that unmet need was the most common reason, followed by pediatric disease as the main indication and PMDA suggestion/request.
- After the revision of the regulation (PFSB/ELD Notice No. 0831-16), seven companies sought to confirm the extension of the reexamination period based on pediatric development with the HA. Of the seven, only three were informed that extension of the reexamination period could be expected.



• Of the projects that did not conduct J-P1 or conducted it in parallel with the MRCT, 22 (17%) had set up a Safety Run-in. • The reasons given were that 15 items were set up by themselves as alternatives to not implementing J-P1 and 10 projects were deemed necessary to ensure the safety of the Japanese population.

• 17 items indicated that there was no impact from the setting up the Safety Run-in, and 6 each indicated that there was an impact on the start of enrollment of Japanese patients and that it took time for the global community for agreement.

Plan for Specific-use Drug Designation (SUDD)



Sixty-one of the 884 projects (7%) belong to the specific classification of SUDD (pediatric disease/drug-resistant bacterial infection). However, only three of them applied/plan to apply for SUDD status.

Background information of the 3 projects which have applied/plan to apply for SUDD One project which joined a global study has applied for SUDD and has already been designated.						
	SUDD Status	Category	ТА	In- licensed	New MoA	Global studies
	Applied & designated	New Indication	Anesthesia	Yes	No	Yes
	Plan to apply	New Dosage	Cardiovascular	No	No	No
	Plan to	New	Cardiovascular	No	Voc	Voc

Consultation for Pooled Region acceptancy



Reasons for Not Applying for SUDD and Requests for Improvement



Any requests for improvement of utilization of the "designation of the specific-use drug" program? (free text)

- Ensuring that the designation criteria are easier to understand
- Simple and short process
- Allow preliminary consultation before application

Number of Clinical Studies (Global/ Domestic)



Global vs Domestic by Development Phase FY2021



Submission lag (1/3)



submission in Japan within 3 months is planned in around 59% projects. (51% in 2021)



Submission lag (2/3)



• Japan first or same day submission with US/EU was mainly based on business decision.

• Among the reasons why 1st submission in Japan / same day filing can be done, the proportion "Standard process" is 9/24. (8/20 in 2021, 2/10 in 2020)

• Major Japan specific reasons which caused delay in Japan submission were:

• PMDA opinion affected submission timing (9/25) Additional study/analyses were conducted based on experience of PMDA interaction (1/25)• Preparation of M2.3 or applicant form for Japan (2/25) • Others (Data package differentiation, PMDA consultation etc)

• Confirmatory study (2) PMDA didn't accept study results such as OS and surrogate makers (2) Long term data (1) Analyses for consistency evaluation between overall and Japanese (1) • Submission for concomitant medication (1)

Global Clinical Development in China

Were you requested to perform clinical studies in China before joining global clinical development? YES 9,33%), 37% NO

answer

8,30%

What type of clinical study was done in China before joining global clinical development



- Phase 1 PK study in Chinese living in China was done in 33% of the projects before China joins the global clinical development.
- Dose range finding study in Chinese was not performed in any of the projects before China joins the global clinical development.

Submission lag (3/3)

What kind of steps are implemented to minimize application submission lag? (free description, n=27)

 Upfront CTD preparation / Simplified review or agreement process of CTD / Parallel preparation of CTD with US/EU (14) • Discussion/collaboration with EU/US from early stage of development • Joining MRCT / minimum data package (4)(3)• Nothing special

Are there any system or requirements which need amendment to minimize application submission lag (free description, n=18)

 English CTD should be accepted (10)(3) • Minimize Japanese data Harmonize clinical evaluation methods in clinical study (2)among US, EU, Japan High price for invest from overseas headquarters (1)• Expedited program (such as RTOR) (1) PMDA consultation system (1)