When Are Japanese Patients First Enrolled?

A Review of PMDA Reports for Oncology Drugs Approved in 2020–2025

Keisuke Tada

Biostatistics in R&D, Sanofi, Tokyo, Japan.

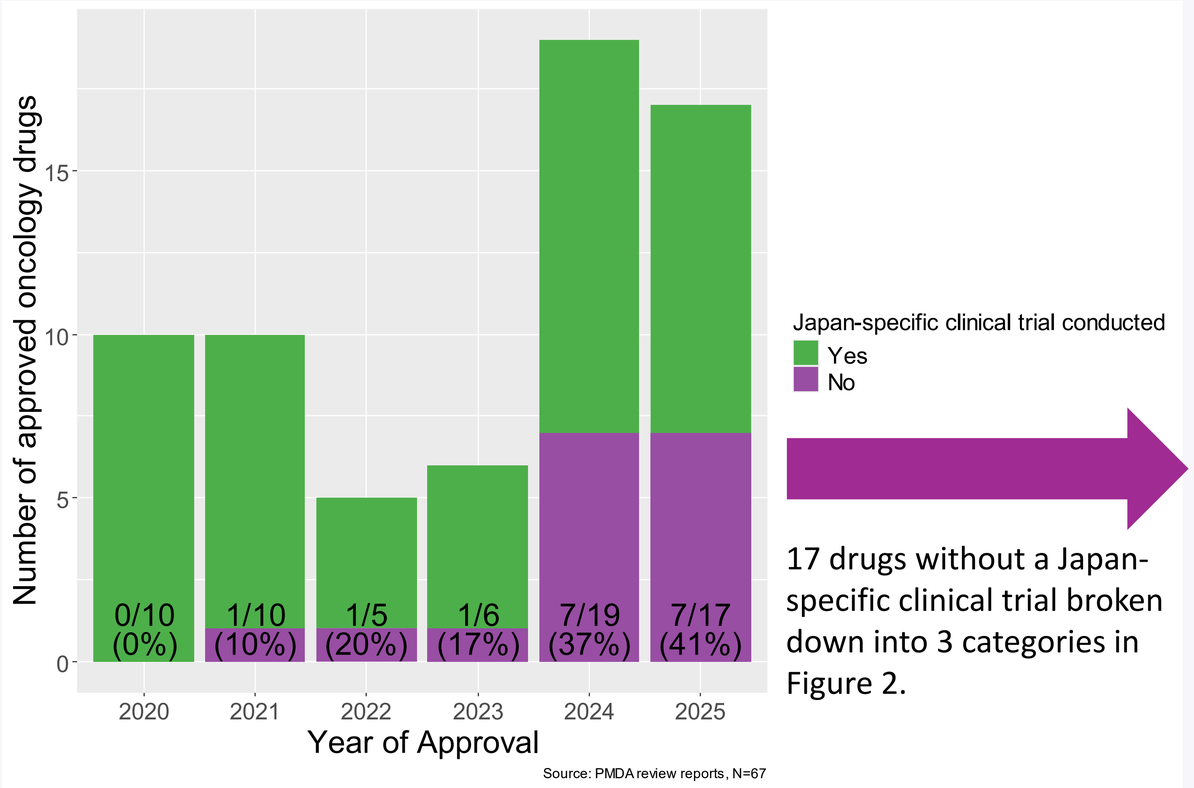
1 Introduction

- Guidance in 2007 “Basic Principles on Global Clinical Trials” → Japanese patients routinely join multi-regional clinical trials (MRCT) for marketing authorization.
- In oncology, sponsors had confirmed the safety and tolerability of investigational drugs in Japanese patients before their participation in registrational clinical trials, traditionally through Japan-specific early-phase clinical trials.
- Participation in early-phase MRCT rather than conduct of Japan-specific early-phase clinical trials has been increasingly observed in recent years.
- Objective: when are oncology drugs first evaluated in Japanese patients during development?

2 Methods

- Investigated 67 PMDA review reports for oncology drugs approved in Japan, 2020–2025.
- Summarized whether a Japan-specific clinical trial was conducted, and if not, the stage of first Japanese enrollment.

3 Results



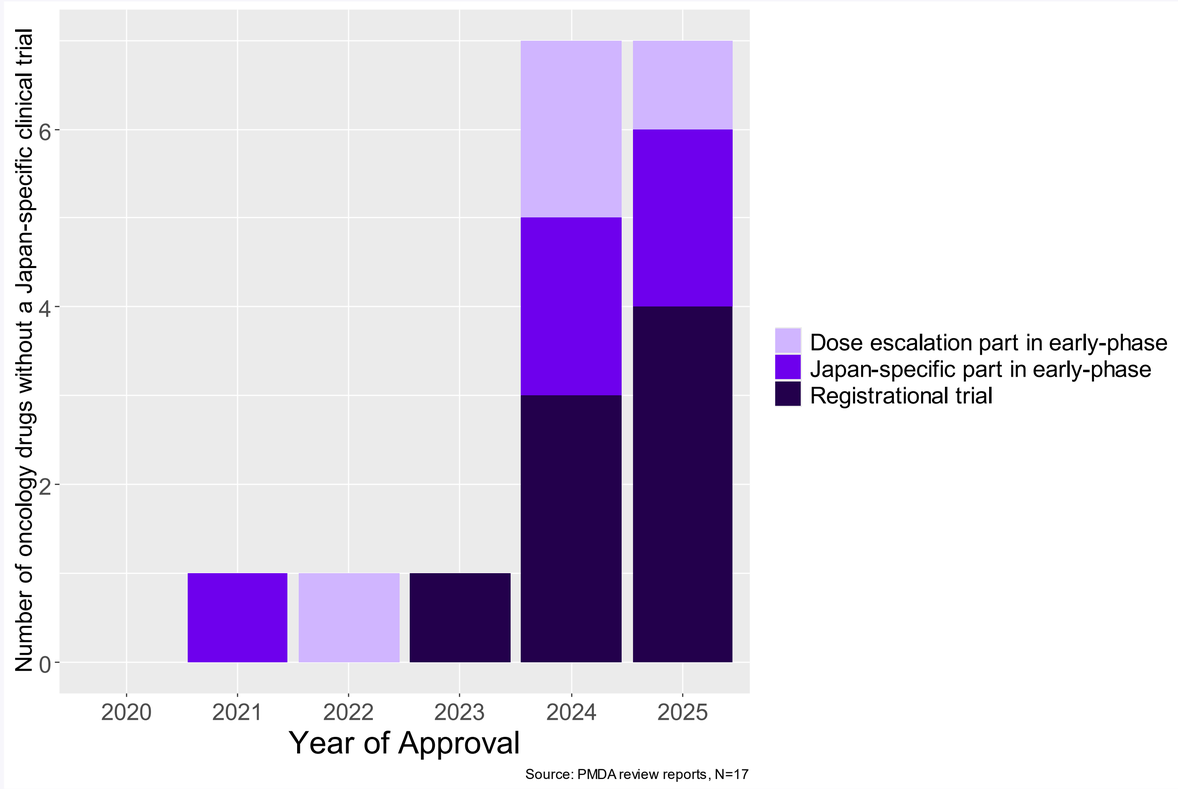


Figure 1. Number of approved oncology drugs by year with/without a Japan-specific clinical trial.
Cochran-Armitage trend test p-value: 0.0043

Figure 2. Stage at which Japanese patients were first enrolled among the 17 drugs without a Japan-specific clinical trial, by approval year.
4 (23.5%) dose escalation in early-phase, 5 (29.4%) via Japan-specific part in early-phase, 8 (47.1%) directly in registrational trials. No drug without a Japan-specific clinical trial was identified in 2020.

4 Discussion

Pros & Cons of options to obtain Japanese data

Option	Pros	Cons	Cost/ Resource†	Regulatory Acceptance†
Conduct Japan-specific early-phase clinical trial	Can fit to all Japanese requirements. Can set specific doses for Japanese patients.	High cost and resource	○	●
Add Japan-specific part/cohort in early-phase MRCT	Relatively easy fit to Japanese requirements. No competitive enrollment. Can set specific doses for Japanese patients.	Additional parts increase cost and workload.	◔	◔
Join MRCT for dose escalation	Can assess patients in Japan and other regions at the same time. No additional cost will be needed, as total number of patients in the clinical trial will not increase.	Not easy to ensure required Japanese patients, as enrollment is competitive. Possible ethnic differences may complicate toxicity assessment.	◑	◕
Join early-phase MRCT after dose escalation	No additional cost will be needed, as total number of patients in the clinical trial will not increase.	Hard to assess dose limiting toxicity in Japanese. Only limited dose levels tested.	◑	◔
Join registrational clinical trial	Low cost and resource	PMDA may request a Japanese safety run-in, delaying enrollment.	●	○

†Author’s qualitative rating: *Less favorable* ○ ◔ ◑ ◕ ● *More favorable*

5 Conclusion

- A higher proportion of recently approved oncology drugs were developed without Japan-specific clinical trials, and for many such drugs Japanese patients were first treated in registrational trials.
- Because approvals reflect development decisions made several years earlier, this shift may continue or grow further, as sponsors continually weigh development efficiency, potential regulatory changes, and other factors.
- Limitations include restriction to approved drugs and reliance on the level of detail in review reports.