Unintended Consequences of the Inflation Reduction Act: Post-Approval Clinical Development in Small Molecule Drugs

James Motyka, PharmD[1]; Julie Patterson, PharmD, PhD[1]; Sharon Phares, PhD, MPH[1]; John O'Brien, PharmD, MPH[1]

[1]National Pharmaceutical Council, Washington, DC, USA

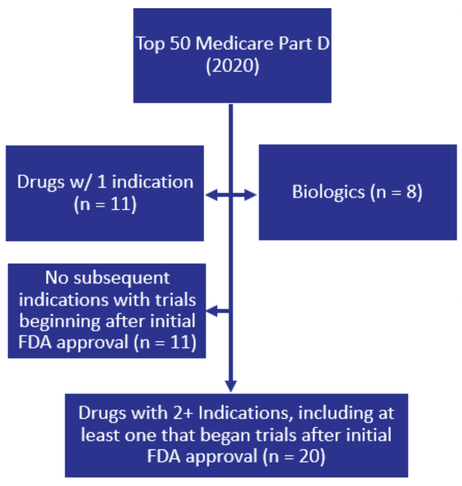
BACKGROUND

- After initial approval by the U.S. Food and Drug Administration (FDA), approximately one-third of drugs undergo clinical trials in new patient populations towards additional indications.[1,2]
- Research into new indications provides patients with expanded treatment options and promotes accessibility by facilitating payer reimbursement.
- The Inflation Reduction Act of 2022 (IRA) introduces price setting for drugs with the highest gross total spending in the Medicare program at 9 and 13 years post-initial FDA approval for small molecules and biologics, respectively.

OBJECTIVE

- To describe the landscape of post-FDA approval clinical development for high-spend Medicare Part D small molecule drugs and illustrate the potential impact of the IRA on research and development (R&D) investments towards subsequent indications.

METHODS



- Brand name, small molecule drugs in the 50 highest gross Medicare Part D spending in 2020 were included if they had at least one additional indication that began clinical trials after initial FDA approval.
- Subsequent indications that began clinical trials - as identified by the posting date to clinicaltrials.gov - after the drug's initial FDA approval were included in the final analytical sample.

RESULTS

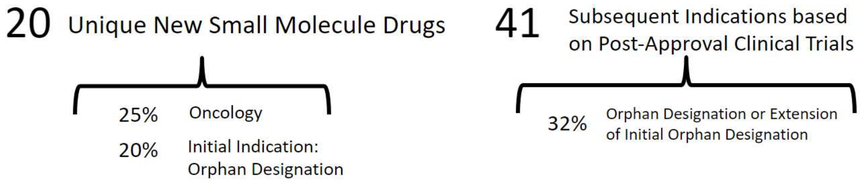


Figure 1. Descriptive Statistics: Drugs Selected for Analyses

- Clinical trials towards a new indication were registered, on average, 3.1 years after initial approval.
- Subsequent indications based on post-approval clinical trials received FDA approval, on average, 7.5 years after a drug was first approved by the FDA.
- Nearly a quarter (n = 10, 24.4%) of the subsequent indications received FDA approval more than nine years after the initial approval.

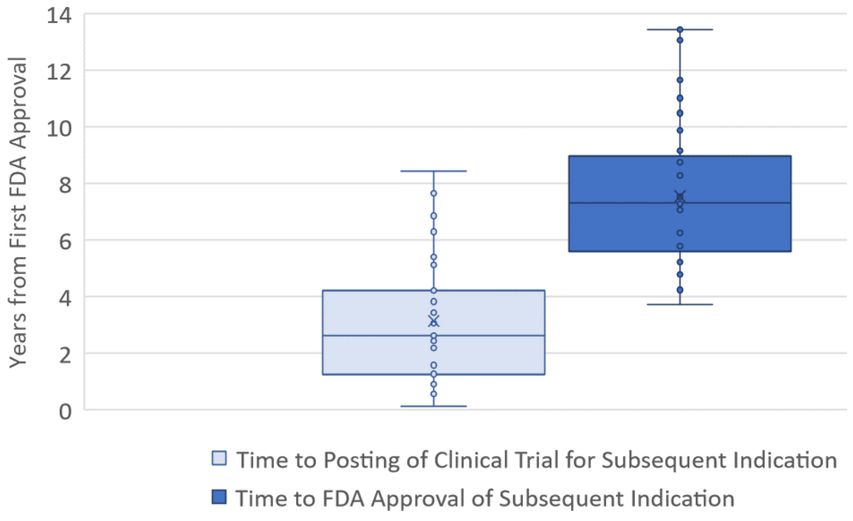


Figure 2. Time from first FDA approval to posting of post-approval clinical trials toward subsequent indications and FDA approval of subsequent indications.

RESULTS (cont.)

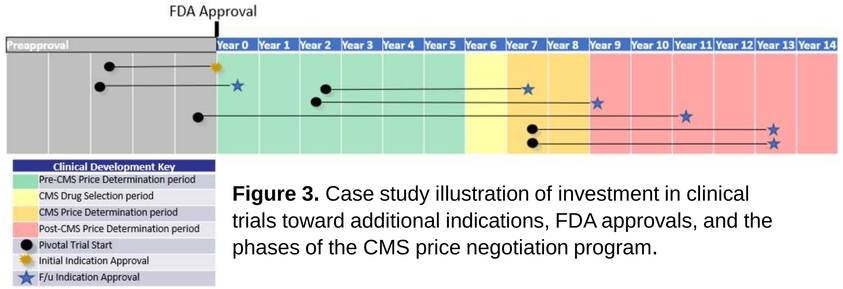


Figure 3. Case study illustration of investment in clinical trials toward additional indications, FDA approvals, and the phases of the CMS price negotiation program.

- The case study above features investments in clinical trials towards additional indications in an oncology product. Pre-approval trials began in three distinct populations, including two different cancers.
- Two indications based on trials that began 2-3 years post-approval were not FDA approved until seven and nine years after the initial approval.
- Another two clinical trials towards subsequent indications began during what is now, under the IRA, the price negotiation period (year 7).

CONCLUSIONS & POLICY IMPLICATIONS

- A significant amount of drug development occurs after initial FDA approval.
- Among drugs studied, post-approval clinical trials started on average 3 years after initial approval, with subsequent indications receiving FDA approval 7.5 years after the drug's initial approval.
- Given the relative timing of post-approval clinical trials, FDA approval, and Medicare's drug pricing negotiation period, the IRA will likely meaningfully reduce manufacturer incentives to invest in clinical trials toward subsequent indications for small molecule drugs, which could result in unintended consequences on patient access to medicines.

REFERENCES

1. Ouimet C, Bouche G, Kimmelman J. Diminishing clinical impact for post-approval cancer clinical trials: A retrospective cohort study. PLoS One. 2022;17(9 September).
2. Sahragardjoonegani B, Beall RF, Kesselheim AS, Hollis A. Repurposing existing drugs for new uses: a cohort study of the frequency of FDA-granted new indication exclusivities since 1997. J Pharm Policy Pract. 2021;14(1).
3. Zhang Z, Zhou L, Xie N, et al. Overcoming cancer therapeutic bottleneck by drug repurposing. Signal Transduct Target Ther. 2020;5(1).
4. Miller KL, Lanthier M. Investigating the landscape of US orphan product approvals. Orphanet J Rare Dis. 2018;13(1).
5. Barbieri JS, St Claire K, Mostaghimi A, Albrecht J. Evaluation of Clinical Compendia Used for Medicare Part D Coverage Determinations for Off-label Prescribing in Dermatology. JAMA Dermatol. 2019;155(3):315-320.
6. Lushin EN, McDermott JK, Truax C, et al. A multicenter case series documenting Medicare Part D plan denials of immunosuppressant drug coverage for organ transplant recipients. American Journal of Transplantation. 2021;21(2):889-896.
7. Wallace ZS, Harkness T, Fu X, Stone JH, Choi HK, Walensky RP. Treatment Delays Associated With Prior Authorization for Infusible Medications: A Cohort Study. Arthritis Care Res (Hoboken). 2020;72(11):1543-1549.
8. Savage KT, Flood KS, Popatia S, et al. Reply to: "Lack of a US Food and Drug Administration indication should not limit access to appropriate treatment." J Am Acad Dermatol. 2019;81(1):e19-e20.
9. Dhodapkar M, Zhang AD, Puthumana J, Downing NS, Shah ND, Ross JS. Characteristics of Clinical Studies Used for US Food and Drug Administration Supplemental Indication Approvals of Drugs and Biologics, 2017 to 2019. JAMA Netw Open. 2021;4(6).
10. Tufts Center for the Study of Drug Development. Protocol Complexity and Patient Enrollment Intensify Challenges in Oncology Trials.; 2021.
11. Angelo de Claro R, Gao JJ, Kim T, et al. U.S. Food and drug administration: initial experience with the real-time oncology review program. Clinical Cancer Research. 2021;27(1):11-14.
12. Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters. Biostatistics. 2019;20(2):273-286.
13. Sahragardjoonegani B, Beall RF, Kesselheim AS, Hollis A. Repurposing existing drugs for new uses: a cohort study of the frequency of FDA-granted new indication exclusivities since 1997. J Pharm Policy Pract. 2021;14(1).