Oncology Drug Development: A Drug-level Analysis of Subsequent Indications

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BACKGROUND

- Post-approval indications of oncology drugs expand treatment options in new cancer types, stages, lines, or combinations.
- New drugs are often first studied in patients with advanced disease who have exhausted available treatment options and later receive indications for earlier lines of treatment.
- The Inflation Reduction Act (IRA) introduced the Medicare Drug Price Negotiation Program, which changes clinical development incentives by authorizing the Centers for Medicare and Medicaid Services to "negotiate" with drug manufacturers the "maximum fair price" of drugs selected from eligible drugs for which at least 7 (small molecule) or 11 (biologic) years have elapsed since their initial FDA approval.

OBJECTIVE

- To describe indication trajectories for new cancers, stages, lines, and combinations in a cohort of recently approved oncology drugs with at least one subsequent indication.

METHODS

- We examined oncology drugs first approved as a new molecular entity drug or original biologic by the FDA from 2008-2018 and later approved for at least one additional indication.
- For each drug, we recorded the type of subsequent indication, including cancer (mutation, gene or protein expression, and histology, if applicable), stage, and line of each indication as well as whether it was approved in combination or as monotherapy.
- We then conducted a drug-level analysis, describing the number and proportion of drugs with subsequent indications of each type as well as the proportion of drugs with each distinct combination of five types of subsequent oncology indications: new cancer; new mutation; new line, new stage; and new combination/monotherapy.

RESULTS

Figure 1. Percentage of Multi-Indication Oncology Drugs with Five Types of Subsequent Oncology Indications

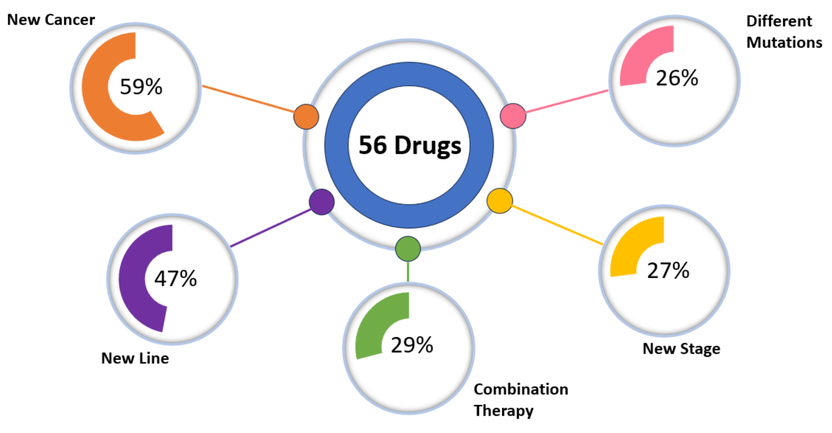
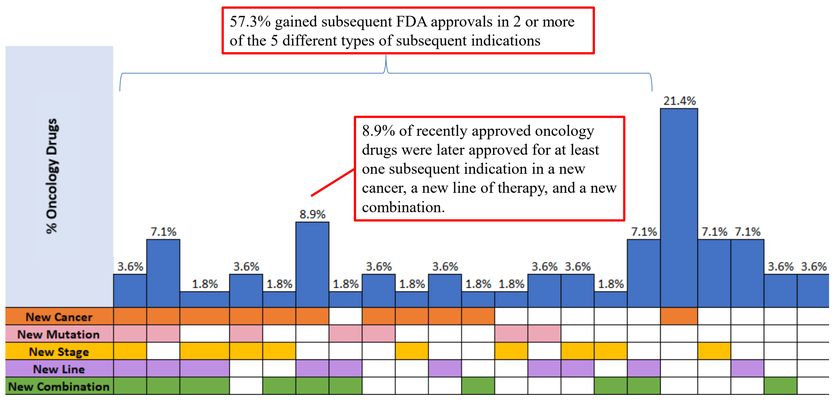


Figure 2. Frequency of Distinct Combinations of Five Types of Subsequent Oncology Indications (N = 56)



RESULTS (cont.)

- A total of 56 oncology drugs (70% small molecule) first approved from 2008-2018 were later approved for at least one subsequent indication (median: 2, IQR: 1-4).
- Most novel oncology drugs were later approved in at least one additional cancer type (59%) (Figure 1).
- Nearly half of drugs (47%) received subsequent indications for at least one new line of treatment for the same cancer and stage.
- Development for new lines and stages were nearly always from later to early lines and most often from more to less advanced stages.
- Most (57.3%) novel oncology drugs gained subsequent FDA approvals in two or more of the five different types of subsequent oncology indications (Figure 2).

CONCLUSIONS & DISCUSSION

- In a cohort of novel oncology drugs, trajectories of FDA approval for subsequent indications demonstrate that drugs often gain approval in additional cancer types, new lines of therapy, and combinations.
- This analysis provides insights into potential unintended consequences of IRA-related changes to the economic incentives surrounding research towards subsequent indications, leading to fewer treatment options for patients with life-threatening diseases.

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