Life years gained from the FDA accelerated approval program in hematology: A portfolio model

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INTRODUCTION

- The FDA Accelerated Approval Program (AAP) was established in 1992 to allow for earlier approval of drugs that treat serious conditions and fill an unmet medical need based on a surrogate endpoint (e.g., response rate). The FDA evaluates and accepts these surrogate endpoints based on scientific evidence.
- A Sponsor must show that a surrogate endpoint is “reasonably likely” to predict clinical benefit, and they must conduct post-marketing studies to verify the clinical benefit. The FDA can withdraw or modify drug approval if these studies fail to verify and describe such effect or benefit, or other evidence demonstrates that the product is not shown to be safe or effective..
- A prior study by the current authors investigated the impact of all cancer accelerated approvals (AAs) between 2006 and 2021, as of their approval status of June 2022 (Benedict et al. 2024). The analysis estimated that the AAP led to approximately 263,000 life-years across 69 products, for about 911,000 patients with cancer. Hematological indications form a large subgroup of therapies approved under the AAP (48 out of 130 in the period examined).

AIM

The objective of this study was to provide an estimate of the population health impact of earlier access enabled by AAP in the US specific to hematology indications. The health impact is estimated in terms of the number of life years gained during the time of earlier access that resulted from the therapies approved via the AAP between January 2006 and June 2021, based on approval status (converted, not yet converted, or withdrawn) and publicly available overall survival (OS) data, as of June 2024.

METHODS

- A decision analytic model was developed to estimate the survival gain for each indication compared with standard of care at the time of approval. The life years gained or lost (depending on the final OS results) were accumulated for consecutive cohorts of patients receiving hematology therapies approved through the FDA AAP between January 2006 to June 2021. **Figure 1** shows the model diagram.
- The model inputs were sourced from FDA listings (Center for Drug Evaluation and Research [CDER] database for the list of AAP indications), drug labels at the time of AA, FDA letters to companies, published clinical trial data, and other publications. Patient uptake of products in the specific AA indications was sourced from the Ipsos Oncology Uptake Tool with data available until December 2022 (i.e., no patient cohorts entered the model after this date). Life year gains were estimated through June 2024 with and without the AAP, and the incremental life years gained were attributed to the program.
- Data on OS for the comparator therapy (standard of care) at the time of the AA and the relative effectiveness estimates for the new therapy were sourced from clinical trial publications. In cases of discrepancy between the AA and the regular approval (RA) trial populations, the change in indications (e.g., a line change or narrower population) were noted, and effort was made to use the efficacy data that is closest to that of the AA indication. For example, if the original approval was in a second-line indication, the analysis used results of the trial completed in the second line, if available, for only patients who received the therapy in the second line, even if the RA study was conducted in the first line.

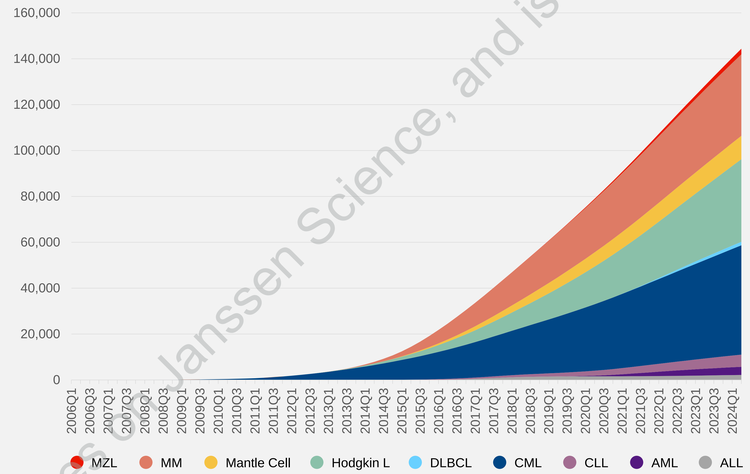
RESULTS

- In the review period (January 2006 to June 2021), 48 hematology indications were approved via the AAP. This number excludes AAs with a dose or solution change, AAs with a revised indication, and products (e.g., chimeric antigen receptor T-cell therapies) not included in the CDER database.
- Among the 48 indications, 24 (50%) obtained RA, 14 (29%) were withdrawn, and 10 (21%) were still ongoing as of March 2024. OS data were identified for 28 indications (21 approved, five withdrawn, two ongoing). Uptake data were available between the AA / RA date for 25 indications.
- The analysis estimated that through June 2024 in the US, 220,557 patients gained approximately a total of 144,381 life years across these 25 products due to the earlier access to therapies. The highest gains were obtained in chronic myeloid leukemia (47,653 life years, 33.0%), Hodgkin lymphoma (36,005 life years, 24.9%), and multiple myeloma (35,514 life years, 24.6%), with further gains in six other cancer types (acute lymphoblastic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, diffuse large B-cell lymphoma, mantle cell lymphoma, marginal zone lymphoma).

Discussion

- Our analysis incorporated hematology indications with an AA regardless of the final approval status, i.e., including all withdrawn indications as well. It calculated the benefit for patients newly starting therapy in the AA indication between AA and RA, and for products that have yet to be approved, for a limited amount of time.

Life Years Gained in Hematology Indications



Abbreviations: ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; CLL = chronic lymphocytic leukemia; CML = chronic myeloid leukemia; DLBCL = diffuse large B-cell lymphoma; MM = multiple myeloma; MZL = marginal zone lymphoma

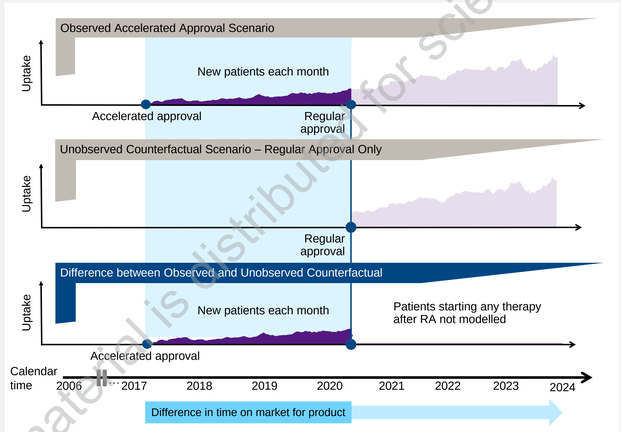
Table 1. Base-case Results by Indication

Cancer type (number of indications)	Life years	Patients
Acute lymphoblastic leukemia (2)	2,193	9,850
Acute myeloid leukemia (1)	3,532	5,492
Chronic lymphocytic leukemia (3)	5,316	8,887
Chronic myeloid leukemia (6)	47,653	100,636
Diffuse large B-cell lymphoma (1)	1,508	2,238
Hodgkin lymphoma (2)	36,005	8,816
Mantle cell lymphoma (1)	10,199	13,468
Multiple myeloma (8)	35,514	61,292
Marginal zone lymphoma (1)	2,460	9,878
TOTAL	**144,381**	**220,557**

Limitations

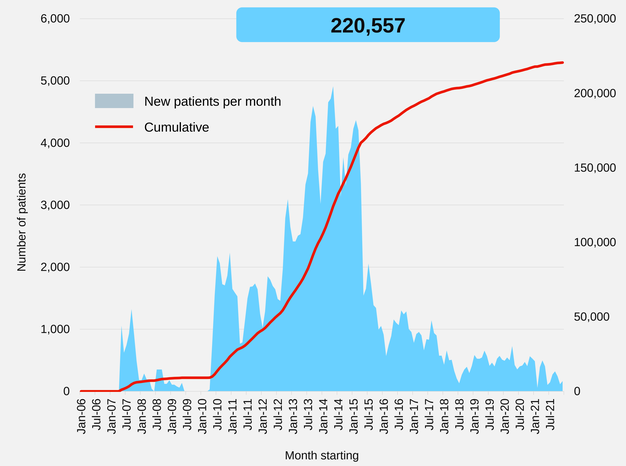
- Limitations of the analysis include the assumption that standard of care remains the same during the AA and RA dates, the use of exponential distribution for modeling survival (over or underestimating life years gained depending on the time course of the hazards for hematology indications with long median survival), missing uptake and OS data for some indications, and not incorporating adverse events, quality of life, or cost of therapies in the analysis. Market uptake is likely underestimated, due to conservative assumptions of the database to scale projections to the US population, and because significant gaps exist in the uptake information for highly beneficial therapies.

Figure 1. Time Horizon, Uptake in Observed and Counterfactual Scenario, and Illustration of Accumulating Life Year Gain of an Indication



Abbreviation: RA = regular approval

Figure 2. Cumulative Number of New Hematology Patients over Time



CONCLUSIONS

Earlier access of drugs to treat serious conditions and fill unmet patient need is the ultimate objective of the FDA AAP. Our research shows that in hematology indications, 220,557 patients gained approximately a total of 144,381 life years due to the earlier access to therapies across hematology products approved between 2006 and 2021.

REFERENCE

Benedict Á, et al. *J Natl Compr Canc Netw*. 2024 Apr 22;22(6):382-389.

Note

In this retrospective real-world evidence study, the likely survival benefit for patients was assessed from the time of initial AA to the time of full traditional approval using OS results from subsequent studies. (Please refer to clinical trials for any specific data related to the survival benefit of an individual therapy.) The results are a snapshot in time specific to the timeframe examined and may not be generalizable for the future.

The Ipsos Oncology Uptake Tool contains historical and current treatment data for multiple oncology indications, derived from the Ipsos Global Oncology Monitor, a physician-reported syndicated patient record database, capturing prescribing of anti-cancer and supportive care agents. Participating physicians are screened for specialty, level of seniority, and number of drug-treated cancer patients seen per study wave and must be the primary decision-maker for their patients. Each wave, participants provide demographic information and de-identified information on a predefined quota of oncology patients (across solid and liquid tumors) seen in consultation, retrospectively. The data used in this poster were collected online in the US from more than 450 oncologists between 2004 and 2022. Sample patient data were projected to the wider clinical population. The Global Oncology Monitor is validated with market sizing studies to ensure that the size and representativeness of the physician sample reflects the wider population of relevant treating physicians.

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