



# Is the number of cancer drug approvals a surrogate for regulatory success?

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## ABSTRACT

Both the speed of approval and efficacy of cancer drugs are important regulatory issues. Although the number of cancer drugs approved in a year is a marker of speed, whether it is also a marker of better outcomes remains unknown. In this study, we assess the trend in number and characteristics of 115 cancer drugs approved by the FDA over the last decade and evaluate whether they have improved patient survival. We find that the number of cancer drug approvals have steadily increased over the years from 5 in 2009 to 33 in 2018. Accelerated approvals started to rise since 2014 and peaked in 2017. The percentage of drugs that improved overall survival has steadily declined and reached its lowest (7 %) in 2017. Approval of better drugs that improve patient outcomes maybe more or at least equally important aspect for regulatory focus compared to approval of more number of drugs.

## 1. Introduction

Cancer being a terminal disease, the speed of drug approvals is an important regulatory and policy issue, along with efficacy of the approved drugs. The U.S Food and Drug Administration (FDA) has the difficult task of balancing the speed of drug approvals with ensuring that the drugs thus approved, actually help improve patient outcomes. The outgoing and incoming FDA commissioners have publicly celebrated the number of cancer drug approvals as a marker of success [1,2]. Although this may represent faster drug approval, whether the number of cancer drug approvals is a valid surrogate for better patient outcomes is unknown. In this study, we assess the trend in the number and characteristics of cancer drug approvals by the FDA over the last decade and evaluate whether these drugs have improved clinical outcomes for the patients.

## 2. Materials and methods

We extracted data on cancer drug approvals over the last decade (2009–2018) from the FDA website (<https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications>). For each approval, we extracted data on the type of approval (accelerated versus regular) and endpoints used for approvals (surrogate versus overall survival). We assessed the trend in drug approvals (number, type and endpoints) over the years. We

included only drug approvals for adult solid tumors in our analysis. We excluded approvals for biosimilars, change in label indications, supportive care, drug withdrawals and diagnostic techniques.

## 3. Results

Over the last decade, we identified 153 drug approvals for adult solid tumors that met our inclusion criteria; 115 were granted regular (75 %) and 38 granted accelerated (25 %) approvals. Seventy-six percent (116) of approvals were based on randomized controlled trials.

The number of drug approvals have steadily increased over the years from 5 in 2009 to 33 in 2018 (Fig. 1). Accelerated approvals started to rise since 2014, peaked in 2017 (40 % of all approvals) but fell to 21 % in 2018. In 2016, 57 % (8/16) of all approvals were based on improvements in surrogate endpoints and not overall survival; this increased to 93 % in 2017 and 85 % in 2018. As shown in figure, this increase in percentage of approvals based on surrogate endpoints was paradoxically accompanied with the decrease in percentage of accelerated approvals, which reflects the increased tendency of the FDA to provide regular approvals based on surrogate endpoints.

The percentage of drugs that have improved overall survival has declined over the decade and reached its lowest in 2017 where only 7 % of drugs approved improved overall survival.

The median overall survival data weren't available for all approvals that improved overall survival. Based on the available information, the

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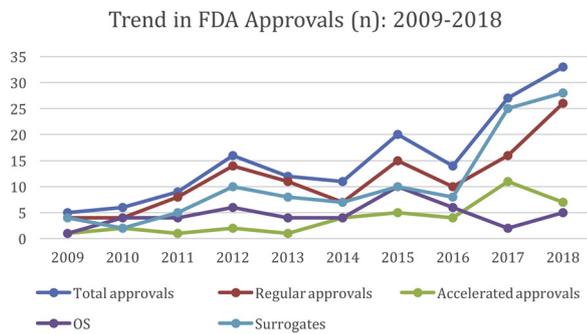


Fig. 1. Trend in FDA approvals of cancer drugs.

median overall survival improvement in 2017 and 2018 were 2.8 (n = 2) and 4.5 months (n = 2) respectively whereas the median overall survival gains over the decade was 2.9 months (n = 38 approvals).

#### 4. Discussion

Although the number of drug approvals for adult solid tumor patients has increased dramatically over the last decade, most of these drug approvals improved only surrogate endpoints with less than one-third of drugs improving overall survival. Surprisingly though, regular approvals have increased more than accelerated approvals in last few years despite the increase in approvals based on surrogate endpoints. It is surprising because the approvals based on surrogate endpoints are usually accelerated approvals and drugs receiving accelerated approvals have a mandate to be tested in confirmatory trials to confirm the clinical benefit [3]. Therefore, this recent trend of granting of regular approvals instead of accelerated approvals based on surrogate endpoints is of concern because unlike accelerated approvals, regular

approvals do not have the requirement for confirmatory post-approval trials.

Approval of more number of cancer drugs is one of the markers of regulatory success. Approval of better cancer drugs that improve outcomes for cancer patients is however the most important marker of regulatory success because cancer patients need better drugs and not just more drugs. This aspect of regulatory approval should be given as much focus by the regulatory authorities as given to the approval of more number of drugs.

#### Disclosures

None.

#### Declaration of Competing Interest

No authors have any conflicts of interest to disclose.

#### Acknowledgments

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#### References

- [1] Gottlieb, S. Twitter. In 2018, FDA approved a record number of novel drugs; including first drug ever to treat smallpox; treatment for management of opioid withdrawal symptoms in adults; many novel cancer therapies; a new class of drugs to prevent migraines; and a new single dose treatment for the flu. Tweet date: 24 Jan 2019.
- [2] Baumann J. Twitter. FDA approved two oncology drugs in 2005; in 2018, there were 48. "To my new colleagues at @US\_FDA, I expect us to keep this up when I get over there," @NCIDirector. #AACR19 #drugapprovals. Tweet date: 31 March 2019.
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