JAMA Network Open

Invited Commentary | Oncology

The Timing of Cancer Drug Approvals in the United States and Europe

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The study by Lythgoe and colleagues[1] provides insights into regulatory processes for cancer drug approvals between the 2 largest medical regulators in the world—the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA).[1] Over the past decade, the FDA approved oncology drugs twice as fast as the EMA, more often through accelerated pathways, and often prior to study publication. Of the 89 cancer medicines approved both in the United States and Europe between 2010 and 2019, the FDA approved 95% (85 of 89) before European market authorization.

The speed of review times and increasing number of FDA-approved cancer medicines has long been used as a metric for successful regulatory processes and improvements in patient outcomes. But do quicker review times result in better outcomes for patients, such as meaningful improvements in survival and quality of life?

Although the speed of FDA review times and subsequent number of approvals have increased over time, the proportion of cancer drugs that improve survival has declined.[2] Furthermore, although other countries approve fewer medicines than the US, available therapies tend to offer more benefit to patients. For example, 48 of 78 drugs (61.5%) recommended by the pan-Canadian Oncology Drug Review—the national Canadian health technology assessment body—demonstrated substantial clinical benefit according to the ESMO Magnitude of Clinical Benefit Scale[3] compared with 43.8% (46 of 105) of FDA approvals within the same period.[4] Similarly, although review times are longer in Europe, data for overall survival is more likely to be available, considerably reducing uncertainty regarding the magnitude of clinical benefit.[5]

The study by Lythgoe and colleagues[1] highlights additional considerations. First, faster review times increase evidential uncertainty and expose patients to additional risk. Lythgoe et al[1] found that more drugs in the US received accelerated approval compared with the EMA and more than one-third are approved prior to study publication.[1] Consequently, more drugs were also withdrawn from the US market. These findings could be interpreted positively; that the system is working as it should. However, the FDA's inconsistent follow-up of postmarketing studies leaves a substantial proportion of cancer drugs approved through accelerated pathways on the market for years without confirmation of their benefit.[6] The FDA Oncology Center of Excellence Center recently announced Project FrontRunner, an initiative to open up the accelerated approval program to earlier lines of treatment.[7] In line with these concerns, newly appointed FDA Commissioner Robert Califf has acknowledged the need to improve postmarket data to support this initiative.[7]

Second, increased speed of US review times lowers global standards for testing and creates a culture of widespread drug access that impose challenges on other countries to obtain the evidence they need for appropriate drug coverage decisions.[8] Cancer drugs are routinely approved using surrogate end points that are often not well correlated with overall survival, increasing uncertainty about the magnitude of clinical benefit. The impact of these FDA practices on other countries are underappreciated. As one Canadian decision maker explained: "the low-bar for FDA approval....makes it very difficult for us to impose an additional bar around what value is it providing and what prices or the cost effectiveness in a culture that wants to use drugs whenever they want to use them."[8] Furthermore, low- and middle-income countries often rely on safety and efficacy assessments from the FDA, a practice called foreign regulatory reliance. Therefore, high levels of uncertainty are passed on to other countries—many without regulatory capacity to withdraw medicines should contradictory evidence arise.[9]

Third, the US has the world's largest pharmaceutical market and is an important country for manufacturers to prioritize. Indeed, Lythgoe et al[1] found that 72% of companies submitted regulatory documents to the FDA before the EMA. This approach might demonstrate a corporate tactic to launch drugs in countries willing to pay higher prices, which in turn increases prices globally. By submitting to the US first, other countries must then negotiate with drug prices that were designed for the unfettered US market.[9] Furthermore, companies are aware that the US is often used in international reference pricing assessments. Therefore, by submitting to the US first, the average price in the basket of reference countries increases, directly raising the prices globally.

A tempting interpretation of the study by Lythgoe et al[1] is that the FDA is a superior agency for expedited review times that bring cancer drugs to patients earlier. However, faster review times have not always translated into better outcomes. In fact, the median survival benefit of new cancer drugs in the US has decreased over time.[2] Compared with Canada and England, the US is less likely to approve medicines based on overall survival data and when they do, the median survival benefit is lower than other countries.[3,5]

Regulatory agencies have the difficult task of balancing earlier patient access to novel treatments and ensuring therapies are effective and safe. However, faster review times and approvals are not cause for celebration; better patient outcomes are. In other words, quality over quantity.

ARTICLE INFORMATION

Published: June 10, 2022. doi:10.1001/jamanetworkopen.2022.16191

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Conflict of Interest Disclosures: None reported.

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