


Balancing Benefit, Risk, and Time to New Cancer Therapies

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The US Food and Drug Administration (FDA) is charged with the task of thoroughly assessing the benefit vs risk of novel therapies. While its representatives may seek greater clarity with more data and longer follow-up, there is a competing challenge of delivering potentially dramatically beneficial new opportunities in the most timely way possible, this pressure perhaps being most acute in the setting of a terminal illness such as advanced non-small-cell lung cancer (NSCLC).

In this issue of *JAMA Oncology*, Kazandjian and colleagues review the process by which the FDA evaluated the immune checkpoint inhibitor nivolumab for patients with chemotherapy-pretreated advanced squamous NSCLC. This summary includes thoughtful discussion of objective response rate (ORR) vs overall survival (OS) as end points potentially sufficient for approval. While very high response rates that far exceed prior benchmarks have led to the admirably rapid approval of crizotinib for anaplastic lymphoma kinase–positive NSCLC based on high response rates in phase II studies, the authors note that the ORR of nivolumab in the CheckMate 063 trial was a modest 15%, a result that may underestimate the incremental value of immunotherapies owing to the unique response patterns of this class of agents. In contrast, OS provided a more meaningful primary end point for the subsequent randomized CheckMate 017 trial.

The report also highlights the steps taken to bring nivolumab to commercial availability as readily as possible once the efficacy and safety of this agent were determined in patients with previously treated advanced squamous NSCLC. This included the FDA decision to defer on formal submission of all safety data from the randomized CheckMate 017 trial and consider prior safety data with nivolumab as well as the expedited review process by the FDA; together, these efforts shortened the time to approval by approximately 6 months. For many appropriate candidates for this agent based on the rapid approval of nivolumab in this setting in early March 2015, this enabled an opportunity to experience a dramatic and prolonged response against a disease for which that time interval is critical.

As the shared enthusiasm of patients and cancer care specialists leads us to complete exciting clinical trials of more immunotherapies and targeted therapies, we remember that our ability to translate the potential benefits to a broader cancer community reaches a potential bottleneck at the doorstep of the FDA. It is very helpful to understand more of the decision-making process and know that the FDA is striving to balance a thorough adjudication of the benefits and risks of these novel strategies with the acute needs of the patients with cancer who cannot afford to wait for them.