The FDA's Pazdur on accelerated approval, single-arm studies, and his own future

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By Adam Feuerstein June 4, 2022

Richard Pazdur is director of the FDA Oncology Center of Excellence. *FDA*

CHICAGO — When cancer drugs granted accelerated approval in the U.S. later turn out not to benefit patients, the Food and Drug Administration would prefer drugmakers remove them from the market voluntarily. But very few companies are willing to do that, which sometimes forces Richard Pazdur, the agency's top cancer drug regulator, to pick up the phone and have a blunt conversation with

drug company executives.

"Peggy Hamburg, a former FDA commissioner, gave me a phrase that I often use — if you don't see the light, you will soon feel the heat," Pazdur said Friday evening, speaking at a STAT event during the annual meeting of the American Society of Clinical Oncology.

In recent years, Pazdur has found himself at the center of a controversy over the FDA's practice of granting accelerated approvals to cancer drugs based on preliminary evidence of efficacy, but before it's determined if the drugs help patients live longer. The program was intended to help cancer patients by getting drugs approved faster, but too often, critics say, the FDA doesn't do enough to force drugmakers to conduct confirmatory studies in a timely fashion. And when certain cancer drugs are later found to be ineffective, it can take years before they're pulled from the market.

Pazdur, whose official title is director of the FDA Oncology Center of Excellence, acknowledged that the accelerated approval of cancer drugs is "under attack," but he deflected blame away from the FDA, saying that the "pain points" in the program are mostly pharma's doing.

"One of the pain points is the industry's over-reliance on single-arm trials," Pazdur said, referring to clinical trials in which all patients receive an experimental drug. Such trials can often give false signals of benefit because they lack a comparator arm.

The FDA has no plans to stop approving cancer drugs based on single-arm studies, but the agency would like their use to be "more selective," Pazdur said.

"For targeted therapies where you have very high response rates, those response rates, we believe, will translate into clinical benefit," he said.

But that's not proven to be true for cancer immunotherapies like the class of treatments known as PD1/PD-L1 checkpoint inhibitors, Pazdur added, noting that response rates do not correlate well at all with an improvement in overall survival.

Pazdur wants the industry to do away with the practice of conducting a single-arm study to secure accelerated approval, and then a separate, randomized study to confirm clinical benefit. A better solution, he said, would be to combine both into a single, randomized study where an interim analysis of response rates could yield fast data to secure accelerated approval, but the trial would continue to eventually collect data on overall survival.

One year ago, the FDA used the accelerated approval pathway for the first time in Alzheimer's disease to grant marketing clearance to Biogen's Alzheimer's treatment Aduhelm. The decision placed the agency under withering criticism from many scientists and FDA watchers, and triggered government investigations. Pazdur had a hand

in the FDA's Aduhelm decision. Asked if he's learned anything from the ensuing Aduhelm backlash, Pazdur declined to go into the specifics of the approval, but said there are things the FDA could do better.

"If you're going to be taking on a new endpoint, you really need to communicate it early and with the community," he said. "Everyone is not going to agree, but you need to give people the chance to comment and get some buy in. And that should be done outside of an application, because once you start with an application, a lot of other issues come into play."

Pazdur has spent more than two decades at the FDA. How long does he intend to remain the agency's top cancer drug regulator?

"Until I drop dead, basically," he said, noting that he's had multiple opportunities to "join pharma land" or do something else — all of which he's turned down.

"I really enjoy the people I work with," he said.

But many of those people do leave the FDA and join the pharma industry.

"Yes, but I call it Dr. Pazdur's finishing school for pharmaceutical executives," he said. "It's one of my greatest joys to see people succeed."

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