PINK SHEET
CITELINE REGULATORY

26 Sep 2024 | **News**

Pazdur Calls For 'Kumbaya' To Standardize ImmunoOncology Biomarkers

by Sarah Karlin-Smith

The US FDA Oncology Center of Excellence head also urged companies to commit to offer their PD-L1 drugs to certain patients free of charge via compassionate use if the gastric and esophageal cancer labeling is modified.

US Food and Drug Administration Oncology Center of Excellence Director Richard Pazdur tried his best to force the leading PD-L1 drug developers to commit to work together and standardize biomarker development for cancer immunotherapies during the 26 September Oncologic Drugs Advisory Committee meeting.

Pazdur has spent years pushing the drug industry to better coordinate development in the checkpoint inhibitor space, although much of his effort was ignored. (Also see "*FDA's Pazdur Advocates Platform Trials For Cancer Drug Development*" - Pink Sheet, 22 Oct, 2019.) and (Also see "*Rx For Immuno-Oncology Excess? Top US FDA Cancer Officials Take On Development 'Wild West'*" - Pink Sheet, 15 Dec, 2021.)

At the 26 September ODAC meeting, Pazdur took a particularly forceful tone on the topic, asking for commitments from *Merck & Co., Inc.*, *Bristol Myers Squibb Company* and *BeiGene, Ltd.* in a

Key Takeaways

- FDA's oncology head Richard Pazdur used the 26 September ODAC meeting to make another push for more coordinated, industry-wide development in the immuno-oncology space, including standardization of future biomarkers.
- Pazdur essentially forced the three sponsors at the meeting to publicly commit to the effort, though it is unclear whether the agency has leverage to

PINK SHEET
CITELINE REGULATORY

manner that seemed to make clear that a "no" would be unacceptable. Whether the agency ultimately has any real regulatory leverage to back up the public accountability is less clear. (Also see "*Complexities of Precision Medicine: Managing Multiple Rx/Dx Combos in the Same Class*" - Pink Sheet, 9 Apr, 2015.)

Pazdur's latest push emerged as the agency considers whether to limit the use of PD-L1 drugs to patients with PD-L1 expression ⩾ 1 for unresectable or metastatic gastric and gastroesophageal junction adenocarcinoma. The committee voted in favor of the move. The overwhelming majority said the risk/benefit assessment of the drugs is not favorable for patients with PD-LD expression <1. (*See sidebar*.)

Merck's Keytruda (pembrolizumab) and Bristol Myers Squibb's Opdivo (nivolumab) currently have labels agnostic of PD-L1 expression in the indications. BeiGene has a pending biologics license application for Tevimbra (tislelizumab) for the indication with a 28 December user fee goal date.

The agency was frustrated when making the current labeling reassessment because even though data across trials and drugs indicates PD-L1 status appears to be predictive of treatment efficacy in the indications, each sponsor used different assays to measure PD-L1 expression and different thresholds to define PD-L1 positivity, making it challenging to compare data across studies.

The presence of multiple drugs, each with their own assays, also creates problems for patient care because a series of tests may be needed to find the best treatment for each patient. (Also see "*Complexities of Precision Medicine: Managing Multiple Rx/Dx Combos in the Same Class*" - Pink Sheet, 9 Apr, 2015.)

enforce it.

- Pazdur also encouraged the sponsors to use expanded access programs to make their immune checkpoint inhibitors available free of charge, if the FDA follows ODAC's advice and restricts the labeling in gastric and esophageal cancers.

All Comers No More? US FDA AdComm Supports PD-L1 Threshold In Esophageal, Gastric Cancer

By Bridget Silverman

26 Sep 2024 Maturing data supporting first-line indications for Merck's Keytruda, Bristol's Opdivo and BeiGene's Tevimbra show inadequate efficacy for patients at the lowest level of PD-L1 expression in esophageal and gastric cancers. *Read the full article here*

The 'Ship Has Sailed,' Pazdur Says

Pazdur acknowledged that the "ship has sailed," when Merck representatives said the company

would be interested in trying make the current assays interchangeable despite the data suggesting they are not.

Instead, Pazdur seemed intent on ensuring future diagnostics are harmonized with more biomarker development in the immunology space expected.

“Well absolutely, we always tried,” said Scott Pruitt, associate VP of Merck Translational Oncology.

Pazdur interrupted mid-sentence, “So you’re on record, you’ll collaborate with anybody,” he said, seemingly refusing to let the companies off the hook.

He asked BMS “Are you going to collaborate with everybody?

“Put away your own commercial concerns here and like come to a kumbaya with everybody that’s developing a similar type of drug?” Pazdur said.

“We do welcome efforts for harmonization,” said Ian Waxman, BMS VP of late development oncology. “I think our goal here it to simplify the process for patients and physicians, so the process by which we do that is up for discussion.”

Pazdur again interrupted.

“I think we’ve learned from this experience. This has been not a great experience, obviously, having all of these different tests here. And here, again, I want to emphasize we did bring people together. We made a concerted effort to FDA in trying to harmonize these tests with several conferences and telephone calls with Friends of Cancer Research and other external organizations. So, you're on board, right? Okay, BeiGene,” Pazdur said, giving BMS no time to object before moving on to the last sponsor.

BeiGene said it was open to harmonization.

“In looking at new biomarkers we really have to develop platforms across the commercial concerns of companies,” Pazdur said.

Compassionate Use Urged

Pazdur then asked the sponsors, “if, and I underline if, we restrict the labels,” to exclude use in PD-L1 <1, would they be willing to operate an expanded access program that would make the immunotherapies available free of charge to patients who no longer meet the labeling criteria for the drug, but are interested in access. Pazdur noted Merck has argued the label should stay agnostic because some patients with low PD-L1 may benefit. (Also see "*US FDA Revisits PD-L1*

Biomarker In Gastric, Esophageal Cancers" - Pink Sheet, 24 Sep, 2024.)

Merck wouldn't commit to an expanded use protocol, saying the company would have to consider it.

"We'll be in contact with you," Pazdur said.

BeiGene said it would be happy to review expanded access requests if physicians felt a particular patient who didn't qualify based on the label would benefit. And BMS said it would look for a mechanism to help patients access a drug if they and their physician believe there would be benefit.

Pazdur seemed to want to be on record reassuring concerned patients and caregivers, particularly given some of the challenges with biopsies and measuring PD-L1, which is a dynamic biomarker that changes over time.

Many of the open public hearing speakers testified in favor of keeping access the same. But advisory committee members said patients with low PD-L1 who were harmed by the drugs may not be alive to testify and the number of patients in this cohort that needed to be treated to find one patient who benefits is high.

"We realize the issues here with biopsy etc. and here again if we do restrict and someone wants the drug it probably would not be paid for [by insurance companies]," Pazdur said. "There might be other avenues that patients may have access to this drug."