Proton Pump Inhibitors May Affect Responses to Tecentriq in Cancer Patients

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Proton Pump Inhibitors May Affect Responses to Atezolizumab in Patients with Urothelial Cancer

Proton pump inhibitor (PPI) use was associated with worse outcomes in patients with urothelial cancer treated with the immunotherapeutic atezolizumab (Tecentriq), compared with patients who did not use PPIs, according to results published in Clinical Cancer Research, a journal of the American Association for Cancer Research.

PPIs are commonly used medications for acid reflux, heartburn, and ulcers. Recent evidence indicates that PPIs cause significant changes to the gut microbiome, which plays an important role in regulating immune function, explained Ashley Hopkins, PhD, an early-career research fellow at Flinders University in Australia. “There is growing concern that an altered gut microbiome could negatively impact the efficacy of immune checkpoint inhibitors,” he said. “Given that approximately 30 percent of cancer patients use PPIs, often for extended time periods, there is an urgent need to determine if PPIs influence the efficacy of immune checkpoint inhibitors.” Five immune checkpoint inhibitors are currently approved in the United States for the treatment of urothelial cancer.

In this study, Hopkins and colleagues evaluated how PPI use impacted survival outcomes in patients with urothelial cancer (commonly referred to as bladder cancer) who were treated with the immune checkpoint inhibitor atezolizumab or with chemotherapy. The researchers examined data from the IMvigor210 and IMvigor211 clinical trials, which evaluated atezolizumab in patients with locally advanced or metastatic urothelial cancer. IMvigor210 was a single-arm study evaluating atezolizumab in previously treated or treatment-naïve patients, while IMvigor211 was a randomized control trial that compared atezolizumab with chemotherapy in previously treated patients.

Of the 429 patients enrolled in IMvigor210 who received atezolizumab treatment, 33 percent had used PPIs within the 30 days before or the 30 days after initiating atezolizumab. In IMvigor211, 31

percent of the 467 patients treated with atezolizumab and 40 percent of the 185 patients treated with chemotherapy had used PPIs within the 60-day window.

Hopkins and colleagues found that among patients treated with atezolizumab, those who used PPIs had a 68 percent greater risk of death, a 47 percent greater risk of disease progression, and a 54 percent lower objective response rate than those who did not use PPIs. PPI use was associated with worse outcomes even after adjusting for several patient and tumor characteristics. In contrast, PPI use did not significantly impact overall survival, progression-free survival, or the objective response rate for patients treated with chemotherapy.

Among PPI non-users, those treated with atezolizumab had a 31 percent lower risk of death than patients treated with chemotherapy. However, among PPI users, there were no significant differences in survival outcomes between patients treated with atezolizumab and chemotherapy, suggesting that PPI use impacted the magnitude of atezolizumab benefit.

“PPIs are overused, or inappropriately used, in patients with cancer by up to 50 percent, seemingly from a perspective that they will cause no harm,” said Hopkins. “The findings from this study suggest that non-critical PPI use needs to be approached very cautiously, particularly when an immune checkpoint inhibitor is being used to treat urothelial cancer.”

A limitation of the study is that it was a retrospective analysis that evaluated a single immune checkpoint inhibitor in one cancer type. Hopkins suggested that future research should evaluate the impact of PPI use on other immune checkpoint inhibitors, additional cancer types, and different combinations of immune checkpoint inhibitors or chemotherapy regimens.

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