# Solid-tumor cancer patients ineligible for clinical trials receive more immunotherapy but may not benefit

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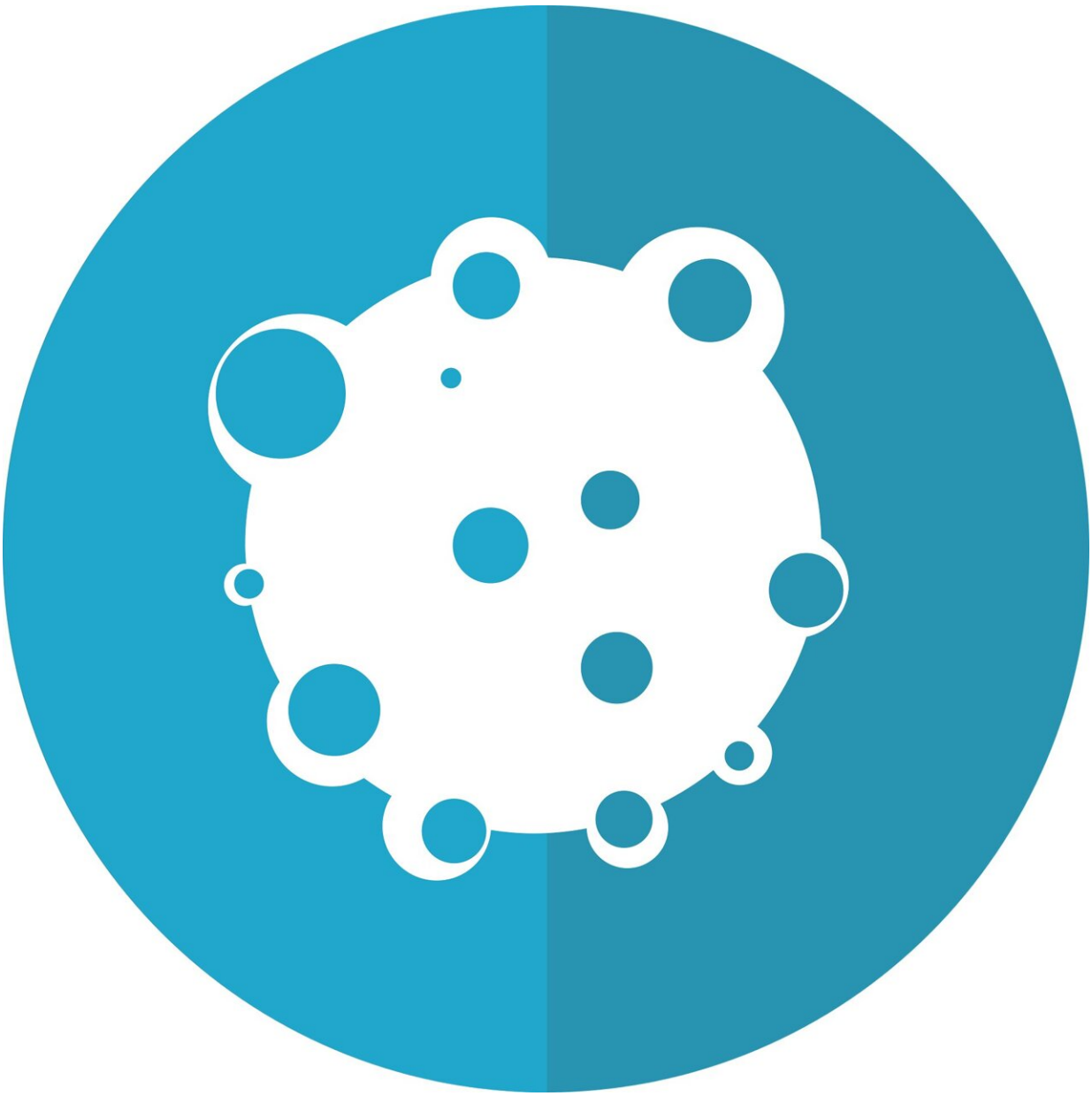

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Cancer patients who are ineligible for clinical trials receive immune checkpoint inhibitors (ICI) at greater rates than patients who are trial eligible despite no survival benefit, according to a new study by researchers at the Perelman School of Medicine at the University of Pennsylvania. The study, published in *JAMA Oncology*, suggests that the positive results for phase 3 clinical trial participants receiving ICI treatment may not translate to patients who are ineligible for trials due to factors such as organ dysfunction.

ICIs, a type of immunotherapy, are part of the standard of care for patients with many advanced solid tumors and are generally associated with improved survival. Randomized phase 3 ICI clinical trials have traditionally excluded advanced cancer patients because of poor performance status—an estimate of a patient's ability to complete daily activities—or disease-related organ dysfunction, which may increase risk for adverse events associated with ICI treatment. Because of the absence of randomized trial data that defines the impact of ICI treatment on advanced cancer patients deemed ineligible for trials, researchers conducted a retrospective study to look at treatment rates and outcomes for these patients, as compared to those patients for whom trial data are available.

The nationwide study of 34,000 patients diagnosed with advanced solid tumors included those with metastatic or recurrent non-small cell lung cancer, urothelial cell cancer, renal cell cancer, and hepatocellular carcinoma. The researchers set out to determine if the frequency of use and effectiveness of ICIs in this patient population with more advanced

disease is similar to those with less advanced disease, as was studied in the clinical trials. They found that use of ICI monotherapy increased over the study period, between 2014 to 2019, up to 30.2 percent among patients who would be trial-ineligible, compared to 19.4 percent among patients who would be trial-eligible.

"Patients with advanced cancers are in desperate need of treatment options, and immunotherapy provides a targeted approach worth studying further, especially in trial-ineligible patients," said Ravi B. Parikh, MD, an assistant professor of Medical Ethics & Health Policy and Medicine at Penn. "Despite the lack of evidence and benefits for this vulnerable population, we found that oncologists used immunotherapy at greater rates for trial-ineligible patients. However, health care providers of patients with poor functional status or organ dysfunction should not assume immunotherapies will confer the same benefit as the populations studied in trials."

The researchers did not find evidence of survival benefit among trial-ineligible patients receiving ICI monotherapy or combination therapy compared to other treatment options, and the study suggests the cautious use of ICI combination therapy for trial-ineligible patients due to the potential for early harm.

"While it makes sense to consider novel therapies like immunotherapies for trial-ineligible patients, it is essential to be alert when using ICI, and to be honest with the limitations of current supporting research to date," said Ronac Mamtani, MD, MSCE, an assistant professor of Hematology-Oncology at the Abramson Cancer Center at Penn. "Even though ICIs have a better side-effect profile for most patients, positive results in phase 3 trials may not necessarily translate to improved quality of life and survival for all patients."

**More information:** Ravi B. Parikh et al, Uptake and Survival

Outcomes Following Immune Checkpoint Inhibitor Therapy Among Trial-Ineligible Patients With Advanced Solid Cancers, *JAMA Oncology* (2021). DOI: 10.1001/jamaoncol.2021.4971