trials reported at two recent medical meetings, the agent achieved statistically significant results in multiple solid malignancies—most notably non–small cell lung cancer (NSCLC).

TIGIT is a receptor expressed on natural killer cells and T cells. It inhibits immune-cell activity by binding to the PVR ligand on tumor and antigen-presenting cells, and its expression strongly correlates with that of PD-1.

Thus, researchers hypothesized "that anti-TIGIT antibodies, which prevent TIGIT from binding to its ligand, could restore the antitumor response and could complement the activity of anti–PD-L1/ PD-1 antibodies," said Melissa Johnson, MD, of the Sarah Cannon Cancer Institute in Nashville, TN. This hypothesis, she added, is supported by preclinical data suggesting that anti-TIGIT plus anti–PD-L1 agents synergistically improve tumor control and prolong survival compared with either antibody alone.

A phase Ia/Ib trial tested tiragolumab in solid cancers. Alone, the drug led to stable disease in four of 24 patients; together, tiragolumab plus atezolizumab elicited responses in three of 49 patients—including a partial response in head and neck squamous cell carcinoma and partial and complete responses in NSCLC. In an expansion cohort, seven of 14 patients with metastatic PD-L1–positive NSCLC responded to the combination. Results were reported by Johanna Bendell, MD, also of Sarah Cannon, at the American Association for Cancer Research Virtual Annual Meeting II: June 22–24, 2020.

Building on those results, Johnson and her colleagues launched the phase II CITYSCAPE trial, which enrolled patients with newly diagnosed locally advanced or metastatic NSCLC who expressed PD-L1 in at least 1% of tumor cells and did not have *EGFR* or *ALK* alterations. Patients were randomly assigned to receive tiragolumab plus atezolizumab or atezolizumab alone. Johnson reported on 135 patients at the 2020 American Society of Clinical Oncology Annual Meeting, May 29–31.

The combination arm had an overall response rate (ORR) of 37% and a median progression-free survival (PFS) of 5.6 months, compared with 21% and 3.9 months in the atezolizumab arm. This difference was linked to PD-L1 expression: Patients in the combination group with PD-L1 expression of at least 50% had an ORR of 66% and did not reach median PFS, compared with 24% and 4.1 months in the atezolizumab group. In contrast, patients in the combination group with lower PD-L1 expression had an ORR of 16% and a median PFS of 4 months, compared with 18% and 3.6 months in the atezolizumab group.

More than 96% of patients in both groups experienced side effects. In addition, 69% of patients treated with the combination experienced immune-related adverse events—most commonly rash and infusion-related reactions—compared with 47% of patients receiving atezolizumab.

The phase III SKYSCRAPER-01 trial is currently investigating tiragolumab plus atezolizumab in patients with newly diagnosed NSCLC and PD-L1 expression of at least 50%. Early-phase trials are also exploring tiragolumab in cervical cancer and small cell lung cancer, as well as blood cancers.

"What has generated a lot of buzz is the objective response rate seen, which is mainly driven by the PD-L1–high group," said Grace Dy, MD, of Roswell Park Cancer Institute in Buffalo, NY, who provided commentary on the phase II trial. Median PFS also favored the combination, she added, also due to PD-L1–high patients. She cautioned, however, that "while we are all excited by the data and want to see a winner, we should be careful."

Cross-trial comparisons are difficult, Dy said, yet it is worth noting that the atezolizumab control group fared significantly worse than the control groups of other phase III trials in NSCLC, which could have magnified the benefit. She also said she wants to know whether favorable or unfavorable mutations were distributed evenly between groups. For example, preclinical data suggest that DNM1 expression maximizes the effect of TIGIT blockade and may correlate with MHC class I expression.

"Nonetheless," she concluded, "we are cautiously optimistic that the combination is a promising advancement."
–*Catherine Caruso* ■

NOTED

The FDA approved the selective oncogenic transcription inhibitor lurbinectedin (Zepzelca; PharmaMar/Jazz Pharmaceuticals) for adults with metastatic small cell lung cancer who have received platinum-based chemotherapy. The approval, the first for the agent, was based on a phase II basket trial in which 105 patients had an overall response rate of 30% and a median duration of response of 5.1 months.

AbbVie will pay Genmab $750 million up front in a deal that could be worth up to $3.2 billion more in milestone payments. Together, the companies will develop and commercialize three of Genmab's early-stage bispecific antibody candidates, including the CD3/CD20-targeting agent epcoritamab, a CD3x5T4 antibody, and a drug that targets CD37.

Tepotinib may be effective in patients with advanced NSCLC who have *MET* exon 14 skipping mutations (N Engl J Med 2020 May 29 [Epub ahead of print]). In a single-arm phase II study, 46% of 152 patients responded to the drug, and responses lasted a median of 11.1 months.

In a series of talks at the American Association for Cancer Research (AACR) Virtual Annual Meeting II: June 22–24, 2020, **researchers discussed the underrepresentation of minority patients in clinical trials.** Ajay Nooka, MD, MPH, of Emory University in Atlanta, GA, spoke about efforts there to increase participation of Black patients in multiple myeloma trials, and Ruben Mesa, MD, director of the Mays Cancer Center in San Antonio, TX, outlined work in southern Texas to improve accrual of Hispanic patients in all types of cancer trials. Among their strategies: partnering with community-based organizations, providing patients with culturally specific educational materials, and educating clinicians about barriers to trial participation.

Also at the AACR meeting, Jean-Yves Pierga, MD, PhD, of the Institut Curie in Paris, France, spoke about the UCBG COMET trial, which compared the prognostic value of circulating tumor cells with circulating tumor DNA for metastatic breast cancer. He concluded that **the two approaches are more complementary than overlapping**, with both biomarkers providing independent prognostic information and biological insights.

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/CDNews.