Tecentriq Plus Avastin Slows Kidney Cancer Progression

Immunotherapy combo was more effective and better tolerated for first-time treatment.

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Combining the checkpoint inhibitor Tecentriq (atezolizumab) and the targeted therapy Avastin (bevacizumab) led to slower disease progression and fewer severe side effects than another commonly used first-line treatment for advanced kidney cancer, according to study findings presented at the American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium this week in San Francisco.

Progression-free survival—meaning study participants were still alive without worsening of their disease—was 11.2 months for patients with a favorable biomarker who received Tecentriq plus Avastin, compared with 7.7 months for those treated with the older targeted drug Sutent (sunitinib).

“For an aggressive cancer like this, where less than 20 percent of people survive five years after diagnosis, we think a 3.5 month longer progression-free survival, given the tolerability for this new combination treatment regimen, is an important development,” lead study author Robert Motzer, MD, of Memorial Sloan Kettering Cancer Center said in an ASCO press release.

Kidney cancer is one of the 10 most common cancers in the United States. Around 63,300 people will develop kidney cancer and nearly 15,000 people will die from it this year, according to the American Cancer Society. Most will develop renal cell carcinoma (RCC), a cancer that starts in the small tubules in the kidney that filter blood and produce urine.

Motzer presented findings from the Phase III IMmotion151 trial, which compared Tecentriq plus Avastin versus Sutent for previously untreated people with advanced of metastatic (spread beyond its original site) renal cell carcinoma.

Tecentriq is a checkpoint inhibitor that blocks the PD-L1 protein on cancer cells or immune cells inside tumors. PD-1 is an immune checkpoint, a receptor on T cells that plays a role in regulating immune function. Some tumors can hijack PD-1 to turn off immune responses against them. Drugs that block the interaction between PD-1 and its binding partner PD-L1 can release the brakes and restore T-cell activity.

Avastin is a monoclonal antibody that works by blocking vascular endothelial growth factor (VEGF), a protein that promotes the proliferation of new blood vessels to supply growing tumors (a process known as angiogenesis) and plays a role in immune suppression. Sutent is a tyrosine kinase inhibitor that blocks receptors for VEGF as well as other growth factors. Because it interferes with multiple cellular processes, it can cause a variety of side effects.

This international study enrolled 915 participants starting in 2015. Around 70 percent were men and the median age was about 60. They were receiving kidney cancer medication for the first time, but most had previously undergone surgery to remove a kidney.

Tissue testing showed that 40 percent had PD-L1 positive tumors, defined as PD-L1 expression on at least 1 percent on tumor-infiltrating immune cells. PD-L1 expression has been assumed to predict better response to PD-1 or PD-L1 checkpoint blockers, but in fact some people with high PD-L1 levels respond poorly while some with PD-L1 negative cancer respond well.

Study participants were randomly assigned to receive Tecentriq at 1,200 milligrams and Avastin at 15 milligrams per kilogram by IV infusion every three weeks, or Sutent pills (50 mg daily) taken for four weeks followed by two weeks off. Patients were followed for a median of 15 months.

Looking at just the PD-L1 positive patients as assessed by the study investigators, progression-free survival (PFS) was 11.2 months for those receiving Tecentriq plus Avastin and 7.7 months for those receiving Sutent—a 26 percent reduction in the risk of disease progression. The difference was smaller when considering the entire study population: 11.2 months versus 8.4 months, respectively, or a 17 percent risk reduction.

Among the PD-L1 positive patients, the overall response rate as assessed by the investigators—meaning complete or partial tumor shrinkage—was 43 percent with Tecentriq plus Avastin versus 35 percent with Sutent. Of these, 9 percent and 4 percent, respectively, were complete responses. In addition, about a third of patients in both groups had stable disease. Overall response rates were somewhat lower in the entire study population: 37 percent versus 33 percent, respectively.

Motzer noted that an independent review committee judged the PFS duration to be shorter and the overall response rate to be lower compared to the investigators' assessments, especially for the PD-L1 positive group. Neither the investigators nor the IRC reviewers were aware of the patients' PD-L1 status.

The median duration of response for PD-L1 positive patients was 12.9 months in the Sutent group, but it could not be determined in the Tecentriq plus Avastin group because a majority of patients (65 percent) were still responding.

Looking at the entire study population, overall survival was not reached in either treatment group because a majority of patients were still alive. But Motzer said preliminary results were "encouraging," suggesting that survival may turn out to be longer in the Tecentriq plus Avastin group with further follow-up.

This study, the first to evaluate a checkpoint inhibitor plus an angiogenesis inhibitor, “points to a combination of both as being highly effective in delaying cancer growth, and there’s an early trend toward improving survival,” ASCO expert Sumanta Pal, MD, of City of Hope told reporters during a pre-conference presscast.

Most people in both treatment groups experienced side effects, but severe adverse events were less frequent in the Tecentriq plus Avastin group (40 percent) compared with the Sutent group (54 percent); 12 percent and 8 percent, respectively, stopped treatment for this reason. Overall, people taking Tecentriq plus Avastin went more than twice as long before experiencing symptoms that interfered with activities of daily living.

Diarrhea, nausea, vomiting, mouth sores and hand-foot syndrome (pain and rash on the palms and soles) were more common with Sutent, while protein in the urine (a sign of kidney dysfunction) was more common with Tecentriq plus Avastin. Five patients in the Tecentriq plus Avastin group and one person in the Sutent group died during the study.

Checkpoint inhibitors work by restoring immune responses against cancer cells, but they can also activate the immune system more broadly and cause excessive inflammation of healthy tissue. Motzer reported that 16 percent of people treated with Tecentriq plus Avastin were treated with corticosteroids to manage immune-related adverse events—less than the proportion seen in prior combination immunotherapy studies.

These findings support Tecentriq plus Avastin as a first-line treatment option for patients with PD-L1 positive advanced renal cell carcinoma, the researchers concluded.

“The side effects of atezolizumab plus bevacizumab were decidedly less harsh thansunitinib,” Motzer said. “And because progression-free survival was also better, I am confident that this relatively easy-to-administer combination will be a strong treatment choice in all medical practices.”

Click here to read the GU18 study abstract.

Click here to read the ASCO press release about the study.
