Tecentriq Plus Chemotherapy Slows Progression of Advanced Lung Cancer

Immunotherapy combo reduced the risk of disease progression or death in a Phase III study.

September 25, 2018 By Liz Highleyman

Initial treatment with Tecentriq (atezolizumab) plus Alimta (pemetrexed) and platinum-based chemotherapy improved progression-free survival for people with nonsquamous non-small-cell lung cancer in the IMpower132 trial, according to a report at the 19th World Conference on Lung Cancer this week in Toronto.

The study showed that the Tecentriq combination performed significantly better than chemotherapy alone, meaning the difference was probably not attributable to chance.

Non-small-cell lung cancer (NSCLC), which accounts for more than 80 percent of all lung cancers, is often detected late and has a high mortality rate. About 234,000 people will be diagnosed with lung cancer and about 154,000 will die from it this year, according to the American Cancer Society.

Tecentriq, from Genentech, is a checkpoint inhibitor that blocks the PD-L1 protein on cancer cells or immune cells in 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.

Vassiliki Papadimitrakopoulou, MD, of MD Anderson Cancer Center in Houston, presented findings from IMpower132, one of several Phase III studies testing Tecentriq with other medications for first-line lung cancer treatment. Tecentriq is currently approved as follow-up treatment for people with metastatic NSCLC who experience disease progression during or following platinum-based chemotherapy.

As reported at the American Association for Cancer Research (AACR) meeting in April, the IMpower 150 study showed that initial treatment with Tecentriq, carboplatin and paclitaxel chemotherapy, and Avastin (bevacizumab)—a VEGF inhibitor that interferes with the growth of blood vessels—reduced the risk of disease progression or death in people with nonsquamous NSCLC that had metastasized, or spread beyond the lungs.

IMpower 132 enrolled 578 people with newly diagnosed Stage IV metastatic nonsquamous NSCLC. They had not yet received chemotherapy and did not have known EGFR (epidermal growth factor receptor) or ALK (anaplastic lymphoma kinase) driver mutations that would make them eligible for targeted therapies. People with untreated brain metastases and those who had previously used immunotherapy were excluded. There was no restriction based on PD-L1 level. Higher PD-L1 levels are associated with better response to checkpoint inhibitors but do not reliably predict response in individual patients.

Participants in this open-label study were randomly assigned to receive Alimta (a chemotherapy drug that interferes with the production of DNA building blocks) and platinum-based chemotherapy (cisplatin or carboplatin) either alone or with Tecentriq. They were initially treated with the full regimen on the first day of a three-week cycle for four or six cycles, followed by Alimta alone or Alimta plus Tecentriq as maintenance therapy for those who experienced clinical benefit.

After about 15 months of follow-up, the overall response rate—meaning complete or partial tumor shrinkage—was 42 percent for people receiving Tecentriq plus chemotherapy, compared with 30 percent for those receiving chemotherapy alone.

People in the Tecentriq group had significantly longer progression-free survival than those receiving chemotherapy alone, meaning they were still alive without worsening of disease (7.6 versus 5.2 months, respectively). This represents a 40 percent reduction in the risk of disease progression or death. Progression-free survival rates at 12 months were 33.7 percent in the Tecentriq arm and 17.0 percent in the chemotherapy-only arm. Tecentriq was associated with better outcomes at all PD-L1 expression levels. Even those who tested negative for PD-L1 saw a 3.6-month gain in progression-free survival.

People in the Tecentriq group had numerically better overall survival, living 4.5 months longer (18.1 versus 13.6 months, respectively). The difference was not statistically significant in this interim analysis, but these data are not yet mature and follow-up is ongoing.

At the AACR conference, researchers reported results from the Keynote 189 trial showing that a similar first-line regimen using Merck's PD-1 checkpoint inhibitor Keytruda (pembrolizumab) plus Alimta and platinum-based chemotherapy led to significant improvement in both progression-free survival and overall survival.

Treatment in IMpower 132 was generally safe, although adverse events were common. About 54 percent of people in the Tecentriq group and about 39 percent of those using chemotherapy alone had severe side effects. Immune-related adverse events are a concern with checkpoint inhibitors. In addition to restoring immune responses against cancer cells, these drugs can also take the brakes off the immune system more broadly, which can lead to excessive inflammation of healthy tissue. No new safety problems were identified in this study.

"The findings from IMpower132 indicate that the addition of atezolizumab to a backbone of carboplatin and pemetrexed chemotherapy provides better clinical efficacy than carboplatin and pemetrexed alone," Papadimitrakopoulou said. "By inhibiting the interaction of PD-L1 with its

receptors PD-1 and B7.1, atezolizumab restores tumor-specific T-cell immunity, offering a valuable treatment option that prolongs survival for patients with Stage IV non-squamous NSCLC.”

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