FDA Approves Atezolizumab in Combination With Bevacizumab and Chemotherapy for First-Line Treatment of Metastatic, Nonsquamous NSCLC

By The ASCO Post
Posted: 12/7/2018 10:54:43 AM
Last Updated: 12/7/2018 10:54:43 AM

On December 6, 2018, the U.S. Food and Drug Administration (FDA) approved atezolizumab (Tecentriq) in combination with bevacizumab (Avastin), paclitaxel, and carboplatin for the first-line treatment of patients with metastatic, nonsquamous non–small cell lung cancer (NSCLC) with no *EGFR* or *ALK* genomic tumor aberrations.

IMpower150

Approval was based on the IMpower150 trial, an open-label, randomized (1:1:1), three-arm trial that enrolled 1,202 patients receiving first-line treatment for metastatic, nonsquamous NSCLC. A total of 1,045 patients (87%) were identified as not having *EGFR* or *ALK* tumor mutations. The trial was designed to conduct comparisons between each of the atezolizumab-containing arms with the control arm. Patients were randomly assigned to receive one of the following regimens:

- Atezolizumab, carboplatin, paclitaxel, and bevacizumab (four-drug regimen)
- Atezolizumab, carboplatin, and paclitaxel (three-drug regimen)
- Carboplatin, paclitaxel, and bevacizumab (control arm).

Following completion of four or six cycles of carboplatin and paclitaxel, patients continued to receive bevacizumab in the four-drug arm and the control arm and continued to receive atezolizumab in the two experimental arms until disease progression or unacceptable toxicity. The major efficacy measures were overall survival and progression-free survival.

Among patients with nonsquamous NSCLC without an *EGFR* or *ALK* mutation, the estimated median overall survival was 19.2 months for patients receiving the 4-drug regimen and 14.7 months for those receiving carboplatin, paclitaxel, and bevacizumab (hazard ratio [HR] = 0.78, 95% confidence interval [CI] = 0.64–0.96; *P* = .016). The estimated median progression-free survival was 8.5 months for patients receiving the 4-drug regimen and 7.0 months for those in the control arm (HR = 0.71, 95% CI = 0.59–0.85; *P* = .0002). The overall response rates were 55% in the 4-drug arm and 42% in the control arm. No significant differences in interim overall survival or final progression-free survival were observed between the three-drug arm and the control arm.

The most common adverse reactions (reported in ≥ 20% of patients) with atezolizumab administered with carboplatin, paclitaxel, and bevacizumab were fatigue/asthenia, alopecia, nausea, diarrhea, constipation, decreased appetite, arthralgia, hypertension, and neuropathy. Atezolizumab was discontinued for adverse reactions in 15% of patients; the most common adverse reaction resulting in discontinuation of atezolizumab was pneumonitis (1.8%).

Antidrug Antibodies

The incidence of development antibodies to atezolizumab ranges from 30% to 42% across clinical studies supporting the approved indications. Among 364 patients with NSCLC who received the 4-drug regimen in the IMpower150 study, 36% (n = 132) had treatment-emergent antibodies against atezolizumab, with the majority (83% of these 132 patients) having antidrug antibodies prior to receiving the second atezolizumab dose. Patients who tested positive for treatment-emergent antidrug antibodies had lower systemic atezolizumab exposure compared to those who were antidrug antibody–negative.

In an exploratory analysis, the hazard ratio for overall survival was similar in the antidrug antibody–positive (0.69; 95% CI = 0.44–1.07) and the antidrug antibody–negative subgroups (0.64; 95% CI = 0.46–0.90). The presence of antidrug antibodies neither increased the incidence nor severity of adverse reactions. Given the high rate of antidrug antibodies, Genentech has agreed to conduct analyses across the atezolizumab development program to evaluate the effects of antidrug antibodies on efficacy, safety, and pharmacokinetics.

The recommended atezolizumab dose is 1,200 mg intravenously over 60 minutes every 3 weeks. View the full prescribing information for atezolizumab.

The content in this post has not been reviewed by the American Society of Clinical Oncology, Inc. (ASCO®) and does not necessarily reflect the ideas and opinions of ASCO®.