By Devon Schuyler

Pembrolizumab Receives Regular Approval in Metastatic Nonsquamous NSCLC

On August 20, the US Food and Drug Administration (FDA) granted regular approval to pembrolizumab (Keytruda, Merck) for use in combination with pemetrexed (Alimta, Lilly) and platinum as first-line treatment for patients who have metastatic nonsquamous non–small cell lung cancer (NSCLC) without endothelial growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations.

Pembrolizumab previously received accelerated approval for this indication in May 2017 on the basis of improvements in overall response rate (ORR) and progression-free survival (PFS) in the KEYNOTE-021 study. The recent approval is based on results of KEYNOTE-189, in which 616 patients receiving first-line treatment for metastatic nonsquamous NSCLC were randomly assigned in a 2:1 ratio to receive pemetrexed and either cisplatin or carboplatin plus either pembrolizumab or placebo. Treatment continued until disease progression, unacceptable toxicity, or a maximum of 24 months.

In a prespecified interim analysis, overall survival (OS) was significantly longer in the pembrolizumab group than in the placebo group (hazard ratio [HR], 0.49; 95% CI, 0.38-0.64; *P*<.00001). At the time of the data cutoff, the median OS was not reached in the pembrolizumab group vs 11.3 months in the placebo group. PFS also was significantly longer in the pembrolizumab group than in the placebo group (HR, 0.52; 95% CI, 0.43-0.64; *P*<.00001). Median PFS was 8.8 months in the pembrolizumab group and 4.9 months in the placebo group.

The ORR was significantly higher with pembrolizumab than with placebo (48% vs 19%; *P*=.0001), and the median duration of response was longer (11.2 vs 7.8 months).

The most common adverse reactions in KEYNOTE-189 were fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, and pyrexia.

Nivolumab Approved for Previously Treated Metastatic SCLC

On August 16, the FDA granted accelerated approval to nivolumab (Opdivo, Bristol-Myers Squibb) for patients with progression of metastatic SCLC after platinum-based chemotherapy and at least one other line of therapy. The agent had already been approved for use in patients with previously treated metastatic NSCLC.

Approval was based on the demonstration of a durable ORR in a subgroup of patients from CheckMate 032, an open-label trial in patients with metastatic solid tumors. This subgroup consisted of 109 patients with metastatic SCLC who had disease progression after platinum-based chemotherapy and at least one other prior line of therapy, regardless of tumor programmed death ligand 1 (PD-L1) status. All patients received nivolumab every 2 weeks until disease progression or unacceptable toxicity.

The ORR with nivolumab was 12% (95% CI, 6.5%-19.5%). Among the 13 patients who responded, the responses lasted for at least 6 months in 77%, at least 12 months in 62%, and at least 18 months in 39%. The responses were unrelated to PD-L1 tumor status.

The most common adverse reactions among 245 patients with metastatic SCLC in CheckMate 032 were fatigue, decreased appetite, musculoskeletal pain, dyspnea, nausea, diarrhea, constipation, and cough. Nivolumab was discontinued because of adverse reactions in 10% of patients, and at least one dose was withheld in 25% of patients because of an adverse reaction. Serious adverse reactions occurred in 45% of patients. The most frequent (≥2%) serious adverse reactions were pneumonia, dyspnea, pneumonitis, pleural effusion, and dehydration.

Additional Approvals

- On August 16, the FDA approved lenvatinib capsules (Lenvima, Eisai) for the first-line treatment of patients with unresectable hepatocellular carcinoma.
- Also on August 16, the FDA updated the prescribing information for pembrolizumab and atezolizumab (Tecentriq, Genentech) to require that an FDA-approved companion diagnostic test be used to determine PD-L1 levels in tumor tissue from patients with locally advanced or metastatic urothelial cancer who are ineligible for cisplatin. The FDA approved a separate companion diagnostic test for each of these agents.
- On August 8, the FDA approved mogamulizumab-kpkc (Poteligeo, Kyowa Kirin) for adults with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy.
- On July 31, the FDA approved lusutrombopag (Mulpleta, Shionogi) for thrombocytopenia in adults with chronic liver disease who are scheduled to undergo a medical or dental procedure.