HEM/ONC News

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Tisotumab Vedotin-tftv Approved for Recurrent or Metastatic Cervical Cancer

On September 20, the US Food and Drug Administration (FDA) granted accelerated approval to tisotumab vedotin-tftv (Tivdak, Seagen) for adults with recurrent or metastatic cervical cancer that has progressed during or after chemotherapy. Tisotumab vedotin-tftv is a tissue factor–directed antibody.

Approval was based on the open-label, single-arm innovaTV 204 trial, which enrolled 101 patients who had recurrent or metastatic cervical cancer and had received no more than 2 prior systemic regimens in the recurrent or metastatic setting. Tisotumab vedotin-tftv was administered at a dosage of 2 mg/kg every 3 weeks until disease progression or unacceptable toxicity. The confirmed objective response rate (ORR) with tisotumab vedotin-tftv was 24%, with a median duration of response (DOR) of 8.3 months.

The most common adverse events (AEs), including laboratory abnormalities, with tisotumab vedotin-tftv were decreased hemoglobin, fatigue, decreased lymphocytes, nausea, peripheral neuropathy, alopecia, epistaxis, conjunctival AEs, hemorrhage, decreased leukocytes, increased creatinine, dry eye, increased prothrombin international normalized ratio, prolonged activated partial thromboplastin time, diarrhea, and rash. The drug has a boxed warning for ocular toxicity.

Cabozantinib Approved for Previously Treated Differentiated Thyroid Cancer

On September 17, the FDA approved cabozantinib (Cabometyx, Exelixis) for the treatment of patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior vascular endothelial growth factor receptor (VEGFR)-targeted therapy. Patients must be ineligible for or have disease that is refractory to treatment with radioactive iodine.

Approval was based on results from the phase 3 COSMIC-311 trial, which enrolled 258 patients with radioactive iodine–refractory DTC that had progressed after up to 2 prior VEGFR-targeted therapies. Patients were randomly assigned in a 2:1 ratio to 60 mg of cabozantinib or placebo once daily. After a median follow-up of 10.1 months, the median progression-free survival (PFS) was significantly longer in the cabozantinib group than in the placebo group, at 11.0 vs 1.9 months, respectively.

The most common AEs with cabozantinib were diarrhea, palmar-plantar erythrodysesthesia, fatigue, hypertension, and stomatitis.

Cabozantinib was first approved in 2016 for the treatment of advanced renal cell carcinoma.

Mobocertinib Approved for NSCLC With EGFR Exon 20 Insertion Mutations

On September 15, the FDA approved mobocertinib (Exkivity, Takeda) for adults who have locally advanced or metastatic non–small cell lung cancer (NSCLC) with epidermal growth factor receptor exon 20 insertion mutations that has progressed during or after platinum-based chemotherapy. The FDA simultaneously approved a companion diagnostic test to identify patients with this mutation.

The approval was based on a phase 1/2 trial of 114 patients with platinum-pretreated NSCLC who received oral mobocertinib at 160 mg. The confirmed ORR with mobocertinib was 28%, the median DOR was 17.5 months, the median overall survival was 24 months, and the median PFS was 7.3 months.

The most common AEs with mobocertinib were diarrhea, rash, nausea, stomatitis, vomiting, decreased appetite, paronychia, fatigue, dry skin, and musculoskeletal pain. The drug has a boxed warning for QTc prolongation and torsades de pointes, as well as warnings and precautions regarding interstitial lung disease/pneumonitis, cardiac toxicity, and diarrhea.

Zanubrutinib Approved in Waldenström Macroglobulinemia and MZL

Zanubrutinib (Brukinsa, BeiGene) received approval on August 31 for adults with Waldenström macroglobulinemia (WM) and accelerated approval on September 15 for relapsed or refractory marginal zone lymphoma (MZL).

The WM approval was based on the results of ASPEN, a phase 3 trial in which 201 patients with *MYD88*-mutated WM were randomly assigned to zanubrutinib or ibrutinib (Imbruvica, Pharmacyclics) until disease progression or unacceptable toxicity. In addition, 28 patients whose *MYD88* status was wild-type or unknown received zanubrutinib. The patients who received zanubrutinib had a response rate of 77.5% and an event-free DOR rate at 12 months of 94.4%.

The MZL approval was based on the results of 2 single-arm clinical trials, including MAGNOLIA, a phase 2 trial of zanubrutinib in 66 patients with relapsed or refractory MZL who had received at least one anti–CD20-based regimen. The ORR by computed tomography was 56%, with a complete response rate of 20%.

The most common AEs with zanubrutinib in a pooled safety population of 847 patients were decreased neutrophil count, upper respiratory tract infection, decreased platelet count, hemorrhage, decreased lymphocyte count, rash, and musculoskeletal pain.

Zanubrutinib was first approved in 2019 for adults with pretreated mantle cell lymphoma.