HEM/ONC News

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Osimertinib Approved for First-Line Treatment in Metastatic NSCLC

On April 18, the US Food and Drug Administration (FDA) approved osimertinib (Tagrisso, AstraZeneca) for the first-line treatment of metastatic non–small cell lung cancer (NSCLC) with either of the 2 most common mutations in the epidermal growth factor receptor (*EGFR*) gene.

Approval was based on the multicenter, international FLAURA trial, which was conducted in 556 patients who had unresectable or metastatic NSCLC with an *EGFR* exon 19 deletion or exon 21 L858R mutation and had not received previous systemic treatment for advanced disease. Patients were randomly assigned in a 1:1 ratio to receive osimertinib at 80 mg orally once daily or standard-of-care treatment with gefitinib (Iressa, AstraZeneca) at 250 mg or erlotinib (Tarceva, Genentech/Astellas) at 150 mg orally once daily.

The estimated median progression-free survival (PFS) was significantly longer with osimertinib than with standard of care: 18.9 vs 10.2 months (hazard ratio [HR], 0.46; 95% CI, 0.37-0.57; *P*<.0001). The confirmed overall response rate was 77% with osimertinib and 69% with standard of care, and the estimated median duration of response (DOR) was 17.6 months with osimertinib and 9.6 months with standard of care.

The most common adverse reactions to osimertinib were diarrhea, rash, dry skin, nail toxicity, stomatitis, and decreased appetite. Serious adverse reactions consisted of pneumonia, interstitial lung disease/pneumonitis, and pulmonary embolism.

FDA Approves Adjuvant Dabrafenib/Trametinib in *BRAF*-Mutated Melanoma

On April 30, the FDA granted approval to combination treatment with dabrafenib (Tafinlar, Novartis) and trametinib (Mekinist, Novartis) for the adjuvant treatment of patients with *BRAF*-mutated melanoma and lymph node involvement.

Approval was based on results of the international, multicenter COMBI-AD trial of 870 patients who had stage 3 melanoma with a *BRAF* V600E or V600K mutation and pathologic involvement of at least 1 regional lymph node. Patients were randomly assigned in a 1:1 ratio to receive dabrafenib at 150 mg twice daily and trametinib at 2 mg once daily or 2 forms of placebo for up to 1 year.

The rate of recurrence or death was significantly lower with combination treatment than with placebo, at 38% vs 57% (HR, 0.47; 95% CI, 0.39; *P*<.0001). The estimated median relapse-free survival was not reached for patients who received the combination therapy, compared with 16.6 months for those who received placebo.

The most common adverse reactions in patients who received the combination were pyrexia, fatigue, nausea, headache, rash, chills, diarrhea, vomiting, arthralgia, and myalgia.

Tisagenlecleucel Approved in Relapsed/Refractory Large B-Cell Lymphoma

On May 1, the FDA approved tisagenlecleucel (Kymriah, Novartis) for adults with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy. Tisagenlecleucel is a CD19-directed genetically modified autologous T-cell immunotherapy.

Approval was based on the single-arm, open-label, multicenter phase 2 JULIET trial, which enrolled 68 adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, or DLBCL arising from follicular lymphoma. Eligible patients had been treated with at least 2 prior lines of therapy or had relapsed following autologous hematopoietic stem cell transplant. Patients received lymphodepleting chemotherapy followed by a single infusion of tisagenlecleucel.

The overall response rate was 50%, with a complete response (CR) rate of 32%. After a median follow-up of 9.4 months, the DOR was longer in patients with a best overall response of CR than in those with a best overall response of partial response. Among patients achieving CR, the estimated median DOR was not reached. The estimated median DOR among patients with a partial response was 3.4 months.

The most common adverse reactions to tisagenlecleucel were cytokine release syndrome, infections, pyrexia, diarrhea, nausea, fatigue, hypotension, edema, and headache. The FDA approved tisagenlecleucel with a Risk Evaluation and Mitigation Strategy (REMS).

Additional Approvals

- On April 17, the FDA approved fostamatinib disodium hexahydrate tablets (Tavalisse, Rigel) for treating adults with chronic immune thrombocytopenia that has not responded sufficiently to previous treatment.
- On May 4, the FDA approved the combination of dabrafenib and trametinib for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer who have a *BRAF* V600E mutation and no satisfactory locoregional treatment option.
- On May 4, the FDA approved the use of recombinant coagulation factor Xa, inactivated-zhzo (Andexxa, Portola) to reverse the anticoagulation effects of factor Xa inhibitors in patients experiencing life-threatening or uncontrolled bleeding.