By Samantha Alleman

US Food and Drug Administration Approves Lenvatinib for Hepatocellular Carcinoma

On August 16, 2018, the US Food and Drug Administration (FDA) approved the kinase inhibitor lenvatinib (Lenvima, Eisai) in capsule form for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC). The drug previously received FDA approval for the treatment of differentiated thyroid cancer and renal cell cancer.

The REFLECT trial (A Multicenter, Randomized, Open-Label, Phase 3 Trial to Compare the Efficacy and Safety of Lenvatinib [E7080] Versus Sorafenib in First-Line Treatment of Subjects With Unresectable Hepatocellular Carcinoma) compared the safety and efficacy of lenvatinib with that of sorafenib (Nexavar, Bayer), the treatment standard for HCC at the time of the trial. A total of 954 patients who had not previously received treatment for metastatic or unresectable HCC were assigned to either lenvatinib (8 or 12 mg once daily; n=478) or sorafenib (400 mg twice daily; n=476). The primary endpoint was overall survival.

Lenvatinib was shown to be noninferior, but not statistically superior, to sorafenib for overall survival (median overall survival, 13.6 months vs 12.3 months, respectively; hazard ratio [HR], 0.92; 95% CI, 0.79-1.06). Progression-free survival was also longer in the lenvatinib cohort according to the modified response evaluation criteria in solid tumors (mRECIST) for HCC (median progression-free survival, 7.3 months vs 3.6 months; HR, 0.64; 95% CI, 0.55-0.75; $P<.001$). The overall response rate was higher in the lenvatinib cohort vs the sorafenib cohort (mRECIST, 41% vs 12%). According to the FDA, the most common adverse events among patients treated with lenvatinib were abdominal pain, arthralgia/myalgia, decreased appetite, decreased weight, diarrhea, dysphonia, fatigue, hemorrhagic events, hypertension, hypothyroidism, nausea, palmar-plantar erythrodysesthesia syndrome, and proteinuria.

The recommended lenvatinib dosages for patients with HCC are 12 mg orally once daily in patients with 60 kg or greater actual body weight or 8 mg orally once daily in patients with less than 60 kg actual body weight.

Tofacitinib Receives Approval From European Commission for Ulcerative Colitis

On August 1, 2018, the European Commission approved tofacitinib (Xeljanz, Pfizer) for the treatment of adult patients with moderate to severe active ulcerative colitis who have little or no response to, or are intolerant of, a biologic agent or conventional therapy. The Janus kinase inhibitor is the only therapy approved for this patient population.

The drug has been approved for a regimen of 10 mg twice daily for at least 8 weeks, followed by 5 or 10 mg twice daily. Approval was based on data from three phase 3 studies from the Oral Clinical Trials for Tofacitinib in Ulcerative Colitis Global Clinical Development Program (OCTAVE Induction 1, OCTAVE Induction 2, and OCTAVE Sustain), as well as the ongoing open-label, long-term extension study OCTAVE Open.

The European Commission previously approved tofacitinib in combination with methotrexate for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately or are intolerant to 1 or more disease-modifying antirheumatic drugs (DMARDs), and as monotherapy in cases of intolerance to methotrexate or when treatment with methotrexate is inappropriate. The drug has also been approved by the European Commission in combination with methotrexate for the treatment of active psoriatic arthritis in adult patients who have not responded adequately to, or have been intolerant of, prior therapy with DMARDs.

The FDA expanded the indication for tofacitinib to include adults with moderate to severe active ulcerative colitis in May 2018.

In Brief

A computer trained by artificial intelligence to diagnose diminutive colorectal polyps had a pathologic prediction rate of 98.1%, allowing endoscopists to safely diagnose polyps without the need to resect. Polyps analyzed by computer-aided diagnosis (CAD) with narrow-band imaging had a negative predictive value (NPV) between 95.2% and 96.5%. Polyps assessed by CAD–methylene blue staining mode analysis had a NPV between 93.7% and 96.4%. The primary endpoint was whether CAD with the stained mode produced a NPV of 90% or greater for identifying rectosigmoid adenomas 5 mm or smaller, which is the recommended threshold for a diagnose-and-leave nonneoplastic polyp strategy. *Ann Intern Med.* doi:10.7326/M18-0249.