By Devon Schuyler

Ivosidenib Approved for Relapsed or Refractory Acute Myeloid Leukemia

On July 20, the US Food and Drug Administration (FDA) approved ivosidenib (Tibsovo, Agios) for adults with relapsed or refractory acute myeloid leukemia (AML) who have an *IDH1* mutation. The FDA simultaneously approved the RealTi*m*e IDH1 Assay (Abbott), a companion diagnostic, to select candidates for treatment.

The approval of ivosidenib was based on an open-label, single-arm, multicenter clinical trial that included 174 adults with relapsed or refractory AML and an *IDH1* mutation. Patients received ivosidenib by mouth at a starting dose of 500 mg daily until disease progression, unacceptable toxicity, or hematopoietic stem cell transplant. The median duration of treatment was 4.1 months (range, 0.1-39.5 months). A total of 21 patients (12%) received a stem cell transplant following ivosidenib treatment.

The rate of complete remission (CR) plus CR with partial hematologic recovery was 32.8% (95% CI, 25.8%-40.3%). The median time to response was 2 months (range, 0.9-5.6 months), and the median duration of response was 8.2 months (95% CI, 5.6-12 months). Of the 110 patients who were dependent on transfusions of red blood cells or platelets at baseline, 37.3% became independent of these transfusions during any 56-day post-baseline period.

The most common adverse reactions to ivosidenib were fatigue, leukocytosis, arthralgia, diarrhea, dyspnea, edema, nausea, mucositis, QT prolongation, rash, pyrexia, cough, and constipation.

FDA Expands Ribociclib Indication to Include Premenopausal or Perimenopausal Women

On July 18, the FDA expanded the indication for ribociclib (Kisqali, Novartis) in combination with an aromatase inhibitor to include premenopausal or perimenopausal women with hormone receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative advanced or metastatic breast cancer, as initial endocrine-based therapy. The FDA also approved ribociclib in combination with fulvestrant (Faslodex, AstraZeneca) for postmenopausal women with hormone receptor–positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression during endocrine therapy.

Ribociclib was previously approved for use in postmenopausal women with hormone receptor–positive, HER2-negative advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine therapy. The new indications for ribociclib are based on the randomized, double-blind, placebo-controlled MONALEESA-7 and MONALEESA-3 trials.

The most common adverse reactions to ribociclib are neutropenia, nausea, infections, fatigue, diarrhea, leukopenia, vomiting, alopecia, headache, constipation, rash, and cough.

FDA Expands Enzalutamide Indication to Include Patients With Nonmetastatic CRPC

On July 13, the FDA expanded the indication for enzalutamide (Xtandi, Astellas) to include patients with nonmetastatic castration-resistant prostate cancer (CRPC). Enzalutamide was previously approved for use only in patients with metastatic CRPC.

The new indication is based on the results of the multicenter PROSPER trial, in which 1401 patients were randomly assigned in a 2:1 ratio to either oral enzalutamide or placebo once daily. Patients without a prior bilateral orchiectomy continued to use gonadotropin-releasing hormone.

Metastasis-free survival was significantly longer in the enzalutamide group than in the placebo group, at 36.6 months vs 14.7 months, respectively (hazard ratio, 0.29; 95% CI, 0.24-0.35; $P<.0001$).

The most common adverse reactions that occurred more frequently in the enzalutamide-treated group than in the placebo group were asthenia/fatigue, hot flashes, hypertension, dizziness, nausea, and falls.

Additional Approvals

- On July 30, the FDA approved iobenguane I 131 (Azedra, Progenics) for patients 12 years or older who have pheochromocytoma or paraganglioma that is iobenguane scan–positive, unresectable, locally advanced, or metastatic and who require systemic anticancer therapy.
- On July 10, the FDA approved ipilimumab (Yervoy, Bristol-Myers Squibb) for use in combination with nivolumab (Opdivo, Bristol-Myers Squibb) for patients 12 years or older with microsatellite instability–high or mismatch repair–deficient metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- On June 19, the FDA limited the use of atezolizumab (Tecentriq, Genentech) and pembrolizumab (Keytruda, Merck) in patients with locally advanced or metastatic urothelial cancer who are not eligible for cisplatin-containing therapy.
- On June 27, the FDA approved the combination of encorafenib (Braftovi, Array) and binimetinib (Mektovi, Array) for patients with unresectable or metastatic melanoma who have a *BRAF* V600E or V600K mutation.