HEM/ONC News

By Devon Schuyler

Selinexor Approved for Multiple Myeloma

On July 3, the US Food and Drug Administration (FDA) granted accelerated approval to selinexor (Xpovio, Karyopharm) in combination with dexamethasone for adults with relapsed or refractory multiple myeloma (RRMM). Eligible patients must have received at least 4 prior therapies and have disease that is refractory to at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody. Selinexor is the first selective inhibitor of nuclear export compound.

Approval was based on the results of part 2 of the multicenter, single-arm, open-label STORM study (NCT02336815), which included 122 patients with RRMM who had previously received 3 or more antimyeloma treatment regimens. Among a prespecified subgroup analysis of 83 patients whose disease was refractory to specific agents, the overall response rate to oral selinexor/dexamethasone was 25.3% (95% CI, 16.4%-36.0%), with 1 stringent complete response, 4 very good partial responses, and 16 partial responses. The median duration of response was 3.8 months (95% CI, 2.3-not estimable).

Common adverse reactions included thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

FDA Approves Darolutamide in Nonmetastatic Castration-Resistant Prostate Cancer

On July 30, the FDA approved darolutamide (Nubeqa, Bayer) for use in nonmetastatic castration-resistant prostate cancer (CRPC).

The approval was based on the multicenter, double-blind, placebo-controlled ARAMIS trial (NCT02200614), in which 1509 patients with nonmetastatic CRPC were randomly assigned in a 2:1 ratio to receive either oral darolutamide or matching placebo. Patients who had not undergone a previous bilateral orchiectomy received concurrent treatment with a gonadotropin-releasing hormone analogue.

The median metastasis-free survival, defined as the time from randomization to first evidence of distant metastasis or death from any cause within 33 weeks after the last evaluable scan (whichever occurred first), was 40.4 months in the darolutamide group vs 18.4 months in the placebo group (hazard ratio, 0.41; 95% CI, 0.34-0.50; $P<.0001$). The overall survival data were not mature.

The most common adverse reactions in the darolutamide group were fatigue, pain in the extremities, and rash. Ischemic heart disease and heart failure were more common with darolutamide than with placebo.

Darolutamide received fast-track designation and priority review from the FDA.

FDA Approves Pexidartinib in Tenosynovial Giant Cell Tumor

On August 2, the FDA approved pexidartinib (Turalio, Daiichi Sankyo) capsules for adults with symptomatic tenosynovial giant cell tumor (TGCT) that is associated with severe morbidity or functional limitations, and is not amenable to surgical resection. Pexidartinib is the first systemic therapy to be approved in TGCT.

The approval was based on results from the international, multicenter, double-blind ENLIVEN trial (NCT02371369), in which 120 patients with TGCT that was not amenable to surgical resection were randomly assigned to pexidartinib or a placebo. After 25 weeks of treatment, the overall response rate was 38% in the pexidartinib group vs 0% in the placebo group ($P<.0001$). Of the 23 patients who responded and were followed for at least 6 months after the initial response, 22 saw their response continue for the entire period. In addition, all 13 of the patients who responded and were followed for at least 12 months after the initial response saw their response continue for the entire period.

Common side effects of pexidartinib included increased lactate dehydrogenase, increased aspartate aminotransferase, changes in hair color, increased alanine aminotransferase, and increased cholesterol. Additional side effects included neutropenia, increased alkaline phosphatase, decreased lymphocytes, eye edema, decreased hemoglobin, rash, dysgeusia, and decreased phosphate.

Prescribing information for pexidartinib includes a Black Box Warning about the risk of serious, potentially fatal liver injury. Pexidartinib is available only through a Risk Evaluation and Mitigation Strategy program.

Pexidartinib received breakthrough therapy and orphan drug designation, along with priority review.

Pembrolizumab Gains Several New Indications

The FDA has granted several new indications to pembrolizumab (Keytruda, Merck) over the past few months. The programmed death 1 inhibitor received approval in July for the treatment of patients with recurrent esophageal cancer that expresses programmed death ligand 1. It also received approval in June for patients with previously treated metastatic small cell lung cancer. In April, pembrolizumab was approved for use in advanced renal cell carcinoma and also stage III non–small cell lung cancer. Pembrolizumab was first approved in 2014 for use in melanoma.