FDA News

By Kathryn Turner, PhD

FDA Approves Panobinostat for Relapsed Multiple Myeloma

Panobinostat (Farydak, Novartis) has been approved by the US Food and Drug Administration (FDA) for patients with multiple myeloma who have received at least 2 prior therapies, including bortezomib (Velcade, Millennium Pharmaceuticals) and an immunomodulatory agent. Panobinostat is the first histone deacetylase inhibitor approved for multiple myeloma.

The approval was based on a subset of patients in the randomized phase 3 PANORAMA1 (Panobinostat or Placebo With Bortezomib and Dexamethasone in Patients With Relapsed Multiple Myeloma) trial, published in *Lancet Oncology* in October 2014 by San-Miguel and colleagues.

This subset contained 193 multiple myeloma patients who received at least 2 prior therapies, including bortezomib and an immunomodulatory agent. Patients received bortezomib and dexamethasone with or without panobinostat. Panobinostat was given orally at 20-mg doses on a 21-day cycle. Progression-free survival was longer in the group treated with panobinostat than in the control group (10.6 months vs 5.8 months, respectively). The response rate was also higher in the panobinostat group (59% vs 41%, respectively). Overall survival was not estimated for either group.

The most common side effects of panibostat were diarrhea, fatigue, nausea, swelling in the arms or legs, decreased appetite, fever, vomiting, and weakness. Other serious side effects included thrombocytopenia, lymphopenia, and peripheral neuropathy.

Panobinostat received priority review and orphan product designation, and was approved through the FDA's accelerated approval program.

Nivolumab Receives New Indication for Lung Cancer

Nivolumab (Opdivo, Bristol-Myers Squibb) has received a new indication, for the treatment of patients with advanced or metastatic squamous non–small cell lung cancer (NSCLC) whose disease has progressed on or after platinum-based chemotherapy. Nivolumab is a programmed cell death 1 (PD-1) immune checkpoint inhibitor that was first approved in December 2014 for patients with unresectable or metastatic melanoma.

Approval of nivolumab was based on the CheckMate 017 trial (Study of BMS-936558 [Nivolumab] Compared to Docetaxel in Previously Treated Advanced or Metastatic Squamous Cell Non-Small Cell Lung Cancer [NSCLC]). This phase 3 study randomly assigned 272 previously treated participants to receive either nivolumab (135 patients) or docetaxel (137 patients). Nivolumab was given intravenously at 3 mg/kg every 2 weeks.

Researchers found a 3.2-month improvement in overall survival for patients receiving nivolumab, making this the first study to indicate a survival advantage with a PD-1 inhibitor in lung cancer.

The most common side effects of nivolumab are fatigue, shortness of breath, musculoskeletal pain, decreased appetite, cough, nausea, and constipation. There are also more serious immune-mediated side effects in the lung, colon, liver, kidneys, and endocrine glands.

Nivolumab for NSCLC received priority review from the FDA.

FDA Approves Dinutuximab for Pediatric High-Risk Neuroblastoma

The immunotherapeutic agent dinutuximab (Unituxin, United Therapeutics) has been approved by the FDA as part of a first-line therapy for pediatric patients with high-risk neuroblastoma. The drug was approved as part of a multimodality regimen for patients who responded to induction therapy, making it the first regimen to be approved specifically for neuroblastoma. Dinutuximab is a chimeric monoclonal antibody that binds to ganglioside GD2 on the surface of neuroblastoma cells, thereby causing cell death.

Approval of dinutuximab was based on results from the phase 3 ANBL0032 (Isotretinoin With or Without Dinutuximab, Aldesleukin, and Sargramostim Following Stem Cell Transplant in Treating Patients With Neuroblastoma) trial performed by the Children's Oncology Group. Patients were randomly assigned to receive interleukin-2, granulocyte-macrophage colony-stimulating factor, and isotretinoin with (113 patients) or without (113 patients) dinutuximab. After 3 years, the event-free survival was higher in patients who received dinutuximab (63%) than in those who did not (46%). Overall survival was also improved at 3 years (73% vs 58%, respectively), but median overall survival was not reached for either group.

The most common serious side effects of dinutuximab included infections, infusion reactions, hypokalemia, hypotension, pain, fever, and capillary leak syndrome. Other side effects include pyrexia, thrombocytopenia, lymphopenia, hyponatremia, increased alanine aminotransferase, anemia, neutropenia, urticardia, hypoalbuminemia, and hypocalcemia.