HEM/ONC News

By Devon Schuyler

FDA Approves Pembrolizumab for Metastatic NSCLC

The US Food and Drug Administration (FDA) approved pembrolizumab (Keytruda, Merck) on October 2 for use in metastatic non–small cell lung cancer (NSCLC) that has progressed on other treatments and that is positive for programmed death ligand 1 (PD-L1). Pembrolizumab was previously approved for use in patients with advanced melanoma after treatment with ipilimumab (Yervoy, Bristol-Myers Squibb). The accelerated approval was based on the results of KEYNOTE-001, an open-label study of patients with advanced NSCLC that had progressed despite the use of platinum-based chemotherapy and, if warranted, targeted therapy for mutations in *ALK* or *EGFR*. Pembrolizumab has not yet been shown to improve overall survival (OS) or disease-related symptoms.

Nivolumab Receives Expanded FDA Approval

Nivolumab (Opdivo, Bristol-Myers Squibb) received a new indication on October 9 for use in patients with previously treated metastatic NSCLC. Patients are eligible for nivolumab if their disease has progressed despite platinum-based chemotherapy, and targeted therapy for those with *EGFR* or *ALK* mutations. Nivolumab is now FDA-approved for use in both squamous and nonsquamous metastatic NSCLC, regardless of PD-L1 expression. The approval was based on the results of the phase 3 CheckMate 057 trial, in which nivolumab demonstrated superior OS in previously treated metastatic nonsquamous NSCLC compared with chemotherapy.

Treatment of Cancer During Pregnancy May Be Safe

Treatment of maternal cancer after the first trimester of pregnancy may not be harmful to the fetus, according to a case-control study published online on September 28 in the *New England Journal of Medicine* by Dr Frédéric Amant and colleagues.

The study included 258 children born in Belgium, the Netherlands, Italy, and the Czech Republic. A total of 129 children born to healthy mothers were matched by gestational age to 129 children whose mothers had treated or untreated cancer during pregnancy (the prenatal-exposure group). Of the children in the prenatal-exposure group, 96 (74%) were exposed to chemotherapy, 11 (9%) were exposed to radiotherapy, 13 (10%) were exposed to surgery, 2 (2%) were exposed to other drug treatments, and 14 (11%) were not exposed to any treatment.

The median gestational age at birth for children in the prenatal-exposure group was 36 weeks, and the rate of preterm birth was 61%. By comparison, the general rate of preterm birth in the participating countries was 7% to 8%.

Children in the 2 groups were examined at a median age of 22 months. The researchers found no significant difference in cognitive development between children in the 2 groups based on the Bayley score, and cardiac evaluation of 47 children at 36 months of age showed no abnormalities.

The authors concluded that although the likelihood of prematurity is increased for children of mothers with cancer during pregnancy, the children did not appear to have problems beyond what would be expected with preterm birth. They cautioned that their results cannot be extrapolated to all chemotherapeutic drugs, especially newer ones, and that the follow-up period was too short to pick up cardiac and cognitive problems that might occur later in life.

Cancer Drugs Approved Based on Surrogate Endpoint Often Fail to Show OS Gains

Many cancer drugs are approved based on a surrogate endpoint, such as progression-free survival or response rate. Now, a study finds that more than three-quarters of newer cancer drugs approved based on a surrogate endpoint continue to have no effect or unknown effects on OS several years after approval.

Drs Chul Kim and Vinay Prasad, who published their study as a Research Letter in *JAMA Internal Medicine*, examined all FDA oncology drug approvals over a 5-year period from January 1, 2008, through December 31, 2012. They found that 36 of the 54 drugs were approved based on a surrogate endpoint.

After a median follow-up of 4.4 years, an improvement in OS was established for 5 drugs (14%). Eighteen drugs (50%) failed to improve OS, and 13 drugs (36%) continued to have unknown effects on OS.

The authors concluded that enforcement of postmarketing studies is "of critical importance."