HEM/ONC News

By Devon Schuyler

Rolapitant Approved for Chemotherapy-Induced Nausea and Vomiting

The US Food and Drug Administration approved rolapitant (Varubi, Tesaro) on September 2 for chemotherapy-associated nausea and vomiting (CINV). The agent, which is indicated for use in combination with other antiemetic agents to prevent delayed CINV in adults, is a selective and competitive antagonist of human substance P/neurokinin 1 receptors.

The approval was based on the results of 3 phase 3 clinical trials, each of which randomly assigned between 526 and 1332 patients to receive either rolapitant 180 mg before chemotherapy or a control treatment of a 5-HT_3 receptor antagonist plus dexamethasone. The first 2 trials examined the use of rolapitant in highly emetogenic cisplatin-based chemotherapy, and the third trial examined the use of rolapitant in various moderately emetogenic chemotherapy regimens. All 3 trials found that rolapitant was significantly more effective than the control treatment at resolving CINV in the delayed phase. The rate of complete response was 72.7% vs 58.4% in the first study, 70.1% vs 61.9% in the second study, and 71.3% vs 61.6% in the third study.

The most common adverse reactions with rolapitant were neutropenia, hiccups, abdominal pain, decreased appetite, dizziness, dyspepsia, urinary tract infection, stomatitis, and anemia.

Rolapitant is contraindicated in patients taking the CYP2D6 substrate thioridazine.

Daratumumab Produces Good Safety and Efficacy Results in Myeloma

Single-agent daratumumab to treat relapsed or refractory multiple myeloma produced a favorable safety profile and encouraging efficacy in a phase 1 and 2 study that was published online by Lokhost and colleagues on August 26 in the *New England Journal of Medicine*. Daratumumab is an experimental human IgG1κ antibody directed against CD38, which is overexpressed in multiple myeloma.

The study, which involved patients with multiple myeloma that was refractory to 2 or more prior lines of therapy, consisted of a dose-escalation study and a 72-patient dose-expansion study. In the dose-expansion study, patients had received a median of 4 prior treatments, 79% of patients had disease that was refractory to the most recent therapy received (including proteasome inhibitors and immunomodulators), and 76% of patients had undergone autologous stem-cell transplantation. Patients received daratumumab at a dose of either 16 mg/kg (42 patients) or 8 mg/kg (30 patients) for up to 24 months.

The overall response rate among the patients who received the 16 mg/kg dose was 36%. This included 2 patients who had a complete response and 2 patients who had a very good partial response. The median progression-free survival was 5.6 months, and 65% of the patients with a response had no disease progression at 12 months. The overall response rate among the patients who received the 8 mg/kg dose was 10%.

The most common side effect in the dose-expansion study was infusion-related reactions, which were mild and affected 71% of patients. The most common grade 3 or 4 adverse events were pneumonia and thrombocytopenia.

Writing in an accompanying editorial, Raje and Longo stated that "the single-agent activity of daratumumab, including complete responses, in this patient population is surprising and very encouraging."

Vemurafenib Effective in Relapsed or Refractory Hairy Cell Leukemia

A brief course of vemurafenib (Zelboraf, Genentech/Daiichi Sankyo) is an effective treatment for relapsed or refractory hairy cell leukemia, according to a phase 2 study that was published online on September 9 by Tiacci and colleagues in the *New England Journal of Medicine.*

The study comprised 2 trials of the oral BRAF inhibitor vemurafenib 960 mg twice a day for 16 to 18 weeks. The first trial, which took place in Italy, enrolled 28 patients; the second trial, which took place in the United States, enrolled 26 patients and will be enrolling 10 more.

The overall response rate was 96% in the Italian study after a median of 8 weeks, and 100% in the US study after a median of 12 weeks. The complete response rate was 35% in the Italian study and 42% in the US study. After a median follow-up of 23 months, the median relapse-free survival in the Italian trial was 19 months among those with a complete response and 6 months among those with a partial response. After 1 year, the overall survival rate in the US study was 91%.

Side effects included arthralgia and arthritis, and secondary cutaneous tumors developed in 7 of 50 patients. Most drug-related adverse events were grade 1 or 2.