HEM/ONC News

By Devon Schuyler

FDA Approves Factor IX Agent for Hemophilia B

The US Food and Drug Administration has approved the use of recombinant coagulation factor IX Fc fusion protein (rFIXFc; Alprolix, Biogen Idec) in adults and children with hemophilia B. The product is indicated for the control and prevention of bleeding episodes, in addition to perioperative management of bleeding.

rFIXFc is able to reduce bleeding episodes with injections given a week or more apart, whereas traditional prophylactic therapy for hemophilia B requires that infusions be given at least twice a week. The agent has an extended half-life because the factor IX molecule is linked to the Fc fragment that is found in antibodies.

The approval of rFIXFc was based on results from 2 phase 3 trials. The phase 3 B-LONG (Study of Recombinant Factor IX Fc Fusion Protein in Subjects With Hemophilia B) study of 123 adults and adolescents with severe hemophilia B found that a single infusion of rFIXFc controlled more than 90% of bleeding episodes (NCT01027364). Common adverse effects included headache and oral paresthesia. In Kids B-LONG (Study of Recombinant Coagulation Factor IX Fc Fusion Protein, BIIB 029, in Pediatric PTP Subjects With Hemophilia B), an ongoing study in children, no inhibitors were detected and the increase in half-life was consistent with that seen in adults and adolescents (NCT01440946).

Sildenafil Users at Elevated Risk for Melanoma

Users of sildenafil (Viagra, Pfizer) appear to be at elevated risk for melanoma, according to an analysis of more than 25,000 men from a prospective cohort study. Laboratory studies had previously shown that sildenafil and other phosphodiesterase 5A inhibitors promoted melanoma synthesis and melanoma cell invasion, which is what prompted this study.

The analysis, which appeared in the April 7 online version of *JAMA Internal Medicine* with Wen-Qing Li as the lead author, included data on 25,848 men from the Health Professionals' Follow-up Study who did not have cancer at baseline. The men provided information about the use of sildenafil for erectile dysfunction and about the incidence of skin cancers; diagnoses of melanoma and squamous cell carcinoma were confirmed pathologically.

A total of 142 melanoma cases, 580 squamous cell carcinoma cases, and 3030 basal cell carcinoma cases were identified. Recent use of sildenafil at baseline was associated with an increased risk of developing melanoma; the hazard ratio was 1.84 (95% CI, 1.04-3.22) after adjusting for such factors as physical activity, lifetime number of sunburns, number of moles, hair color, and family history of melanoma. Sildenafil was not associated with an increased risk of squamous cell or basal cell carcinoma. The presence of erectile dysfunction was not associated with melanoma.

Although this was a preliminary, observational study and does not prove cause and effect, June Robinson proposed in an accompanying commentary that primary care physicians make a point of screening older men with a history of sunburns for melanoma when prescribing sildenafil.

Palbociclib Improves PFS in Metastatic Breast Cancer

The experimental agent palbociclib significantly improved progression-free survival (PFS) when used as a first-line treatment for metastatic breast cancer that was estrogen receptor–positive (ER+) and human epidermal growth factor receptor 2–negative (HER2–), according to a phase 2 study presented at the American Association for Cancer Research meeting in San Diego, California (Abstract CT101).

For the study, called PALOMA-1, Richard Finn and colleagues randomly assigned 165 postmenopausal women with ER+/HER2– metastatic breast cancer to receive either palbociclib (125 mg a day for 3 weeks, followed by 1 week off) plus letrozole (Femara, Novartis) or letrozole alone. Treatment continued until disease progression, unacceptable toxicity, or withdrawal of consent.

PFS was significantly higher in the palbociclib/letrozole arm (20.2 months) than in the letrozole-alone arm (10.2 months), with a hazard ratio of 0.488 (95% CI, 0.319-0.748). Patients with elevated expression of cyclin D1 or reduced expression of p16 had been shown in preclinical studies to have improved sensitivity to palbociclib, but in this study, palbociclib did not have an enhanced effect on PFS in patients with 1 or both of these gene alterations. Overall survival was 37.5 months for those who received palbociclib/letrozole and 33.3 months for those treated with letrozole, a statistically nonsignificant difference. The most common adverse events with palbociclib/letrozole were neutropenia, leukopenia, fatigue, and anemia.

Palbociclib is an inhibitor of the cyclin-dependent kinases 4 and 6 that is being developed by Pfizer. It is being studied in phase 3 trials for late-stage, metastatic breast cancers, and in combination with endocrine therapy for certain early-stage breast cancers.