HEM/ONC News

By Devon Schuyler

Eribulin Approved for Unresectable or Metastatic Liposarcoma

The US Food and Drug Administration has approved eribulin (Halaven, Eisai) for patients with unresectable or metastatic liposarcoma who have received prior treatment with an anthracycline-containing regimen. Eribulin is an inhibitor of microtubule dynamics that was first approved in 2010 to treat patients with metastatic breast cancer.

Approval of eribulin in liposarcoma was based on results of a phase 3 trial that was presented by Dr Patrick Schöffski at the 2015 American Society of Clinical Oncology annual meeting. The study randomly assigned 452 patients with leiomyosarcoma or liposarcoma to eribulin or dacarbazine every 21 days until disease progression.

Among the 143 patients with liposarcoma, median overall survival was 15.6 months in the eribulin group and 8.4 months in the dacarbazine group (hazard ratio [HR], 0.51; 95% CI, 0.35-0.75).

Treatment-related adverse events were more common with eribulin than with dacarbazine, including neutropenia (44% vs 24%), pyrexia (28% vs 14%), peripheral sensory neuropathy (20% vs 4%), alopecia (35% vs 3%), and thrombocytopenia (28% vs 6%).

Updated results of this trial were published online in the *Lancet* on February 10.

Caplacizumab Speeds Resolution of Acute Episodes of Thrombotic Thrombocytopenic Purpura

Caplacizumab was found to reduce the time to platelet count normalization and the early exacerbation rate in patients with an acute episode of acquired thrombotic thrombocytopenic purpura (TTP) in a phase 2 study. Caplacizumab is a humanized single–variable domain immunoglobulin that prevents thrombosis by acting against the A1 region of von Willebrand factor.

For the study, which was published in the February 11 issue of the *New England Journal of Medicine*, Peyvandi and colleagues randomly assigned 75 patients with an acute episode of acquired TTP to either caplacizumab (36 patients) or placebo (39 patients) in addition to standard care, which consisted of daily plasma exchange and immunosuppressive therapy. The study drug was continued for 30 days after the final plasma exchange.

The researchers found that the median time to a confirmed platelet response was shorter in the caplacizumab group than in the placebo group: 3.0 vs 4.9 days among the 69 patients who had not undergone a plasma exchange session before enrollment, and 2.4 vs 4.3 days among the 6 patients who had undergone a plasma exchange session. Overall, the median time to response was 39% shorter with caplacizumab than with placebo (P=.005).

Exacerbations occurred in 3 caplacizumab-treated patients (8%) and 11 placebo-treated patients (28%), highlighting the platelet-protective effect of caplacizumab. Relapses during the first month after discontinuation of treatment with the study drug occurred in 8 caplacizumab-treated patients and no placebo-treated patients and were linked to an incomplete resolution of the underlying autoimmune disorder.

As expected, bleeding-related adverse events were more common with caplacizumab than with placebo, affecting 54% vs 38% of patients, respectively. However, these events were considered mild in 83% of patients and moderate in 14% of patients; only 3% were severe. None of the bleeding events required substitution therapy.

The authors concluded that caplacizumab "prevents further platelet aggregation more rapidly than conventional treatment alone, which could potentially prevent short- and long-term end-organ injury due to ischemia."

Primary Care Physicians Ordering Fewer PSA Tests

In October 2011, the US Preventive Services Task Force (USPSTF) released a recommendation against routine prostate cancer screening for men of all ages with the prostate-specific antigen (PSA) test. The recommendation led to a decrease in PSA screening overall, a new study finds, but the decline was steeper among primary care physicians than among urologists.

Zavaski and colleagues, who published their results online February 8 in *JAMA Internal Medicine* as a Research Letter, used records from the National Ambulatory Medical Care Survey to compare the frequency of PSA screening in 2010 with that of screening in 2012. The study included a total of 1222 men aged 50 to 74 years who visited a urologist or primary care physician for preventive care and did not have prostate cancer, elevated PSA levels, benign prostate hyperplasia, prostatitis, or another prostate disorder.

The researchers found that the use of PSA screening decreased from 37% to 16% in visits to primary care physicians (P=.009), and from 39% to 35% in visits to urologists (P=.09).

According to an accompanying Editor's Note, "there seems to be a continued perception, more firmly held by urologists than by primary care physicians, that screening is beneficial."

Neratinib Boosts Invasive Disease–Free Survival in HER2-Positive Breast Cancer

Up to one-quarter of patients with human epidermal growth factor receptor 2 (HER2)–positive breast cancer experience disease recurrence despite treatment with chemotherapy and trastuzumab (Herceptin, Genentech). Now, a study finds that adding neratinib to treatment can improve invasive disease–free survival in these patients. Neratinib is an inhibitor of HER1, HER2, and HER4.

For the phase 3 ExteNET study (Study Evaluating The Effects Of Neratinib After Adjuvant Trastuzumab In Women With Early Stage Breast Cancer), Chan and colleagues randomly assigned 2840 women with early-stage HER2-positive breast cancer to receive either neratinib (1420 patients) or placebo (1420 patients) for 12 months after trastuzumab-based adjuvant therapy. The study was published online February 10 in *Lancet Oncology*.

After a follow-up of 24 months for all patients, invasive disease–free survival events had occurred in 70 patients in the neratinib group and 109 patients in the placebo group (HR, 0.67; 95% CI, 0.50-0.91; *P*=.0091). The invasive disease–free survival rate at 2 years was 93.9% in the neratinib group and 91.6% in the placebo group, a difference of 2.3 percentage points. This difference increased to 4.2 percentage points among the subset of patients with hormone receptor–positive disease, for whom the invasive disease–free survival rate at 2 years was 95.4% with neratinib and 91.2% with placebo.

The most common grade 3 or 4 adverse events with neratinib were diarrhea, vomiting, and nausea. Grade 3 diarrhea occurred in 40% of patients in the neratinib group, and 17% of patients in the neratinib-discontinued the agent because of diarrhea.

According to a Comment by Rugo and Chien that accompanied the article, the evidence of improved outcome with neratinib must be balanced against the increase in toxicity. They pointed out that intensive loperamide prophylaxis, which was not used in this study but has been reported to reduce the rate of grade 3 diarrhea to 0% to 17%, might change this equation.

Lenalidomide Improves Progression-Free Survival in Mantle Cell Lymphoma

Several single-group studies have shown that the immunomodulatory agent lenalidomide (Revlimid, Celgene) has activity in patients with relapsed or refractory mantle cell lymphoma. Now, a randomized phase 2 study has shown that progression-free survival is significantly longer with lenalidomide than with investigator's choice monotherapy in these patients.

The study, which was published online in *Lancet Oncology* on February 15 by Trněný and colleagues, included a total of 254 patients who had mantle cell lymphoma that had relapsed 1 to 3 times, had an Eastern Cooperative Oncology Group performance status of 0 to 2, and were ineligible for intensive chemotherapy or stem cell transplant. Patients, whose median age was 68.5 years, were randomly assigned 2 to 1 to receive either lenalidomide or investigator's choice of single-agent treatment.

After a median follow-up of 15.9 months, median progression-free survival was significantly longer in the lenalidomide group than in the investigator's choice group: 8.7 vs 5.2 months (*P*=.004). The most common grade 3 or 4 side effects were neutropenia and thrombocytopenia.

According to a Comment by Dunleavy that appeared with the article, quality of life was maintained or even improved in the lenalidomide group compared with the investigator's choice group.

"The superior activity and preserved quality of life of lenalidomide over investigator's choice in relapsed or refractory mantle cell lymphoma . . . makes it an attractive treatment option for patients with the disease."

Dunleavy pointed out that the study began before the approval of Bruton's tyrosine kinase inhibitors, which future studies should compare with lenalidomide.

Genetic Variants Linked to Venous Thromboembolism in African Americans

African Americans are 30% to 60% more likely than European Americans to develop venous thromboembolism (VTE) but are unlikely to have well-known risk factors for VTE, such as factor V Leiden. Now, a study has identified 3 genetic variants associated with increased risk of VTE that are found primarily in African Americans.

For the study, which was published online in *Blood* on February 17, Perera and colleagues genotyped DNA samples from 578 African Americans, of whom 146 had a history of unprovoked VTE. After determining which variants were most prevalent, they tested DNA from an additional group of 159 African Americans, of whom 94 had VTE.

The researchers found that 36% of the participants had at least 1 risk variant associated with decreased expression of thrombomodulin: rs2144940, rs2567617, or rs1998081. Having one of these variants was associated with a 2.3-fold increase in the risk for VTE.