PHARMACY CORNER

Pralatrexate Injection Approved for Peripheral T-Cell Lymphoma

Pralatrexate injection (Folotyn™, Allos Therapeutics, Inc.) received accelerated U.S. Food and Drug Administration (FDA) approval for use in the treatment of relapsed or refractory peripheral T-cell lymphoma. Approval was granted based on the PDX 008 trial in which 109 evaluable patients demonstrated an overall response rate of 27%. Median response duration was 9.4 months.

Pralatrexate is a folate analog metabolic inhibitor. Recommended dosing is 30 mg/m^2 IV push over 3–5 minutes once weekly for six weeks followed by a week of rest in each seven-week cycle. Prior to initiating therapy, patients should have a platelet count of 100,000 or greater (50,000 for subsequent cycles) and an absolute neutrophil count of 1,000 or greater. Patients on therapy also require supplementation with 1 mg vitamin B_{12} intramuscular injections every 8–10 weeks and 1–1.25 mg folic acid by mouth daily to help reduce mucositis and hematologic toxicities.

The most common adverse reactions with pralatrexate included mucositis, 70%; thrombocytopenia, 41%; nausea, 40%; fatigue, 36%; anemia, 34%; constipation, 33%; pyrexia, 32%; edema, 30%; cough, 28%; epistaxis, 26%; vomiting, 25%; neutropenia, 24%; and diarrhea, 21%. Of eight deaths that occurred within 30 days following pralatrexate administration, one occurred as a result of cardiopulmonary arrest in a patient with mucositis and febrile neutropenia and may have been related to the use of pralatrexate. The other seven deaths were attributed to disease progression.

For more information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2009/022468lbl.pdf.

Denosumab May Be Alternative to Bisphosphonate Therapy

Denosumab (Amgen Inc.), a human monoclonal antibody, may provide an alternative to bisphosphonate therapy in the prevention of pathologic fractures in patients with skeletal metastases. Denosumab works by targeting the RANK ligand, which is a regulator of the osteoclasts responsible for bone breakdown.

A phase III, randomized, double-blind clinical trial evaluating patients with solid tumors excluding breast and prostate cancer (N = 1,776), sponsored by Amgen Inc., demonstrated noninferiority of denosumab compared to standard therapy with zoledronic acid (Zometa™, Novartis Oncology) in preventing skeletal events. The median time to first skeletal-related event was 20.6 months for patients receiving denosumab 120 mg subcutaneously every four weeks and 16.3 months for patients receiving zoledronic acid 4 mg IV over 15 minutes every four weeks (hazard ratio [HR] = 0.84, 95% confidence interval [CI]: 0.71–0.98). Advantages of denosumab include a less toxic effect on renal function. In addition, denosumab use is not associated with flu-like symptoms often seen with zoledronic acid. In terms of osteonecrosis of the jaw, similar rates were seen in both arms of the study.

In a second phase III trial, also sponsored by Amgen Inc., involving patients with metastatic breast cancer (N = 2,046), denosumab demonstrated superiority over zoledronic acid in extending the time to first skeletal-related event (HR = 0.82, 95% CI: 0.71–0.95).

For more information, visit www.amgen.com/media/media_pr_detail.jsp?releaseID=1334123.

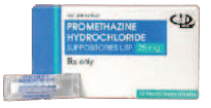
SAFETY CONCERNS

Link Between Chelating Agents and Fatalities Investigated

Iron overload can be a serious consequence of frequent red blood cell transfusions, and iron chelation has been an important component in the management of patients experiencing this complication. Unfortunately, use of chelating agents such as deferasirox (Exjade™, Novartis) comes with its own risks. An ongoing FDA review is examining the potential of increased risk for adverse reactions in patients with myelodysplastic syndrome aged 60 years and older being treated with deferasirox. Serious reactions attributed to deferasirox in older patients with hematologic malignancies include acute renal failure and gastrointestinal hemorrhages. In the presence of concomitant thrombocytopenia, cases also have been reported where gastrointestinal hemorrhage resulted in death.

For more information, visit www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm183840.htm.

Extravasation Risk Added for Promethazine Hydrochloride



The FDA has required the addition of a boxed warning to promethazine hydrochloride (Phenergan™, Wyeth-Ayerst Laboratories) products regarding the risks of extravasation injury when the medication is given via IV. Severe tissue damage, including cases of gangrene leading to amputation, has occurred following extravasation of promethazine via peripheral IV lines. For this reason, the FDA recommends using the intramuscular route when promethazine hydrochloride is required. Subcutaneous injection is contraindicated.

For more information, visit www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm182500.htm.

NOTEWORTHY

Chemotherapy Administration Standards Developed

The Oncology Nursing Society (ONS) and the American Society of Clinical Oncology (ASCO) have collaborated to develop a national set of standards for the safe administration of chemotherapy. Published in both the *Oncology Nursing Forum* and the *Journal of Clinical Oncology*, the standards also can be viewed on the ONS and ASCO Web sites. Nurses should familiarize themselves with the standards to help ensure safety in the chemotherapy ordering and administration process.

For more information, visit www.ons.org/CNECentral/Chemo/Standards.

Blood Test May Help Detect Ovarian Cancer

The FDA has approved a blood test called OVA1™, developed by Vermillion Inc., for use in women aged 18 years and older with pelvic masses who have already been selected to undergo surgery to help identify the likelihood of malignant ovarian cancer. The test makes this determination by looking for changes in five different proteins. The use of presurgical malignancy detection will help determine whether referral to a gynecologic oncologist or surgeon would be appropriate. Because of observed improvements in survival rates, the American College of Obstetricians and Gynecologists and the Society of Gynecologic Oncologists recommend referral to a gynecologic oncologist when malignancies are suspected. OVA1 is not intended as an ovarian cancer screening tool and should only be used in women with pelvic masses who have already been selected to undergo surgery.

For more information, visit www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm182057.htm.

Legislation Aims to Curb Tanning Risk in Teenagers

The association between ultraviolet ray exposure and incidence of melanoma has been well documented. As reported by Pichon et al. (2009), legislation limiting access to tanning beds by teenagers may reduce use and, therefore, risk for the development of melanoma. Calls to 3,647 tanning facilities in 116 cities across the country by data collectors posing as fair-skinned 15-year-old girls who had never tanned revealed that 87% required parental consent. However, only 14% required a parent to accompany the child and a remarkable 71% would allow tanning on a daily basis for the first week. Highlighting the effectiveness of legislation, the authors noted that, in Wisconsin, 70% of facilities stated they would not allow the data collector to tan because it is illegal in that state for teenagers younger than age 16. However, 30% still did not disallow tanning by teenagers, even in the presence of legislation forbidding it.

Pichon, L.C., Mayer, L.A., Hoerster, K.D., Woodruff, S.I., Slymen, D.J., Belch, G.E., . . . Weinstock, M.A. (2009). Youth access to artificial UV radiation exposure: Practices of 3,647 U.S. indoor tanning facilities. *Archives of Dermatology, 145,* 997–1002. doi: 10.1001/archdermatol.2009.85

Carpal Tunnel Syndrome Tied to Breast Cancer Treatment

As reported by Sestak, Sapunar, and Cuzick (2009), use of aromatase inhibitors in postmenopausal women as adjuvant therapy for breast cancer may increase the risk of carpal tunnel syndrome (CTS). In the Arimidex, Tamoxifen, Alone or in Combination trial, women treated with anastrozole (Arimidex™, AstraZeneca) (n = 3,092) had a 2.6% (n = 80) incidence of CTS at the 100-month follow-up. In comparison, women treated with tamoxifen (Nolvadex™, AstraZeneca) (n = 3,092) only had a 0.7% (n = 23) incidence of CTS. It should be noted, however, in both treatment groups the incidence of CTS is rare, and when CTS did occur, it was typically only mild to moderate in severity and of short duration.

Sestak, I., Sapunar, F., & Cuzick, J. (2009). Aromatase inhibitor-induced carpal tunnel syndrome: Results from the ATAC trial. *Journal of Clinical Oncology, 27,* 4961–4965. doi: 10.1200/JCO.2009.22.0236

Technology Promises Improved Patient Communication

As reported by family medicine psychologist Doug Post, PhD, during the International Conference on Communication in Healthcare, use of hand-held personal digital assistants may be a feasible method to improve communication between patients and caregivers. In a pilot study conducted at the Ohio State University Comprehensive Cancer Center–James Cancer Hospital and Solove Research Institute, patients (n = 27) were provided mobile devices on which to record symptoms of pain, fatigue, and depression while on therapy. The symptom reports were then available for physician review during regularly scheduled appointments. The mobile devices also provided a means for teaching patients how to better communicate their symptom experiences. Eighty-three percent of study participants completed the symptom surveys as instructed and, compared to a control group (n = 23), study participants reported a significant reduction in pain severity. Improved communication regarding the pain experience and effectiveness of interventions may have played a role (Ohio State Medical News, 2009).

Ohio State Medical News. (2009). Breast cancer patients track symptoms with digital device. Retrieved from http://medicalcenter.osu.edu/viewer/press/Pages/index.aspx?newsid=5126

PRODUCT UPDATE

Test Determines Potential Tamoxifen Benefit

Tamoxifen remains an important medication in the prevention of estrogen receptor–positive breast cancers. However, even with tamoxifen therapy, many women experience recurrences of their tumors. One factor that has been suggested to impact the effectiveness of tamoxifen is the ability to produce the enzyme CYP 2D6; many women are either unable to produce this enzyme or produce it at lower than normal levels. Genelex Corporation now offers Tamoxitest™ as a diagnostic test to identify patients with a deficiency in CYP 2D6 production. The suggested reason for testing is that patients with CYP 2D6 deficiencies may benefit from alternative therapies. Not all researchers agree that CYP 2D6 status is an important determinant for predicting tamoxifen effectiveness. As discussed by Lash, Lien, Sorensen, and Hamilton-Dutoit (2009), a review of 10 epidemiology studies failed to conclusively demonstrate that tamoxifen is less beneficial in patients with inherited nonfunctional levels of CYP 2D6.

For more information, visit www.tamoxitest.com.

Lash, T.L., Lien, E.A., Sorensen, H.T., & Hamilton-Dutoit, S. (2009). Gentotype-guided tamoxifen therapy. *Lancet Oncology, 10,* 825–833. doi: 10.1016/S1470-2045(09)70030-0

Supplement Offers Nutritional Value to Patients With Cancer

Isopure Co., LLC, offers an option for patients with cancer seeking to increase nutritional intake with its new Isopure Plus Nutritional Drinks™. The 8 oz. supplements come as clear, fruit-flavored beverages containing 190 calories and 15 G of whey protein isolate.

For more information, visit www.isopure.com

Description of products does not indicate or imply endorsement by the *Oncology Nursing Forum* or the Oncology Nursing Society. Michael Smart, RN, BSN, OCN®, can be reached at nursemrsmart@aol.com, with copy to editor at ONFEditor@ons.org.

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