PHARMACY CORNER

Treatment Approved for Rare Pancreatic Tumors

The U.S. Food and Drug Administration (FDA) has approved sunitinib (Sutent®) for use in treating progressive well-differentiated pancreatic neuroendocrine tumors (PNETs) that are locally progressed, metastatic, or unresectable. This is the second drug approved for PNETs in 2011, the first being everolimus (Afinitor®).

Normal dosing for PNET with sunitinib is 37.5 mg PO per day without treatment breaks, which is significantly different from the way other diseases are treated with sunitinib. In treating gastrointestinal stromal tumors and renal cell carcinoma, for example, sunitinib is given in six-week cycles of four weeks on treatment followed by two weeks off treatment.

Sunitinib may be taken with or without food and is metabolized via the CYP3A4 pathway. If strong concomitant CYP3A4 inhibitor or inducers cannot be avoided, dosage modifications should be considered.

Approval in treating PNET was based on a randomized, double-blind, placebo-controlled phase III clinical trial in which patients were randomized to receive sunitinib (n = 86) or placebo (n = 85). Progression-free survival was 10.2 months on treatment compared to 5.4 months on placebo (p = 0.000146). Ninety-two percent of patients in both arms of the study had liver metastases, and most also previously had received another form of systemic therapy.

Nurses should educate patients about common adverse reactions such as fatigue, asthenia, fever, diarrhea, nausea, mucositis, vomiting, dyspepsia, hair color changes, anorexia, and bleeding. As the list of potential toxicities is long, supplementing patient education with written material may be helpful. Because of the potential for liver toxicity and thyroid dysfunction, laboratory values should be monitored. Signs of cardiac toxicity, such as congestive heart failure, should be evaluated and promptly addressed. In addition, because of the effect of sunitinib on vascular growth and wound healing, treatment interruption may be indicated in patients undergoing major surgery.

For additional information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2011/021938s13s17s18lbl.pdf.

New Option Available for *Clostridium Difficile*

Diarrhea associated with *Clostridium difficile* infection (CDI) is a potentially life-threatening condition, and many patients with cancer are at an increased risk for contracting CDI as a result of therapies that suppress the immune system (e.g., chemotherapy) and kill the normal flora of the gastrointestinal tract (e.g., broad-spectrum antibiotics). The main strategies for treating CDI include the use of metronidazole (Flagyl®) and oral formulations of vancomycin. Unfortunately, with both of these treatments, some patients do not have durable responses once treatment is completed, possibly because the spore form of *Clostridium difficile* survives through therapy and resurges at therapy cessation.

A third treatment option, fidaxomicin (Dificid™), has been approved by the FDA based on clinical trial data (N = 1,164) that showed comparable response using fidaxomicin 200 mg PO twice a day compared to vancomycin 125 mg PO four times a day for 10 days. Both strategies demonstrated an almost 90% response rate, but the durability of response at 25 days following initiation of therapy was greater in the fidaxomicin arm. In fact, 70%–72% sustained response in the fidaxomicin arm versus 57% in the vancomycin arm.

The drug works directly in the gastrointestinal tract and is not absorbed systemically. Fidaxomicin generally is well tolerated with minimal side effects. The most common reported adverse effects include nausea, vomiting, headache, abdominal pain, and diarrhea.

For additional information, visit www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm257024.htm.

Investigational Drug Reduces Risk of Death From Melanoma

Targeted therapy shows dramatic promise in the treatment of metastatic melanoma exhibiting the BRAF V600E mutation, which is present in almost half of cutaneous melanomas. As reported by Chapman et al. (2011), a phase III clinical trial (N = 675) comparing the BRAF kinase-inhibitor vemurafenib with dacarbazine demonstrated a 63% relative reduction of risk for death with vemurafenib at six months compared to treatment with dacarbazine ($p < 0.001$). In addition, patients in the vemurafenib group demonstrated a 74% decreased risk for tumor progression or death at six months. Remarkably, 48% of the vemurafenib group experienced confirmed objective responses to therapy compared to 5% in the dacarbazine group ($p < 0.001$).

Only patients exhibiting the BRAF V600E mutation were included in the trial, and those without the mutation should not be expected to have similar responses.

All patients had previously untreated stage IIIC or stage IV melanoma and were randomized to receive vemurafenib 960 mg PO twice a day or dacarbazine 1,000 mg/m^2 IV every three weeks.

Common adverse reactions to vemurafenib included rash, arthralgias, photosensitivity, and fatigue. Eighteen percent (n = 61) of patients in the vemurafenib group developed squamous-cell carcinomas or keratoacanthomas while on treatment, but these were addressed easily by excision and did not require treatment interruption.

Chapman, P.B., Hauschild, A., Robert, C., Haanen, J.B., Ascierto, P., Larkin, J., . . . McArthur, A.G. (2011). Improved survival with vemurafenib in melanoma with BRAF V600E mutation. *New England Journal of Medicine, 364,* 2507–2516. doi:10.1056/NEJMoa1103782

SAFETY CONCERNS

Prostate Medications Increase Risk for High-Grade Disease

The FDA required labeling changes to all FDA-approved 5-alpha reductase inhibitors (5-ARIs) because clinical data indicates that these drugs increase the risk for high-grade prostate cancers (i.e., more aggressive and deadly tumors). The 5-ARIs commonly are used in the treatment of benign prostatic hypertrophy (BPH) to prevent bladder retention by reducing the size of the prostate. The 5-ARIs include finasteride (Proscar®) and

dutasteride (Avodart®). Dutasteride also is found in the combination drug dutasteride and tamsulosin (Jalyn™), which is used to treat benign prostatic hyperplasia, and finasteride (Propecia®), which is marketed in smaller doses for the treatment of hair loss.

The labeling change requirements arose from studies designed to look at the possible risk reduction of prostate cancer with the use of 5-ARIs. Two clinical trials, the Prostate Cancer Prevention Trial (PCPT) and the Reduction by Dutasteride of Prostate Cancer Events (REDUCE), did demonstrate an overall reduction in the risk for prostate cancer with the use of 5-ARIs, but the benefit was seen only in cancers of low risk (i.e., slow growing). Conversely, the incidence of high-grade tumors was noted to increase.

In the PCPT trial (N = 18,882), patients treated with finasteride were noted to have a 26% lower risk of any prostate cancer when compared to placebo ($p < 0.0001$), but when looking at the incidence of high-grade tumors with Gleason scores (GS) of 8–10, a 1.8% incidence occurred in the finasteride arm versus 1.1% in the placebo arm.

In the REDUCE trial (N = 8,231), patients treated with dutasteride were noted to have a 23% lower risk of prostate cancer compared to placebo ($p < 0.0001$), but this was limited to low-risk prostate cancers (GS < 6). The incidence of high-grade tumors (GS = 8–10) doubled from 0.5% on placebo to 1% on treatment.

The FDA issued guidance that 5-ARIs not be used for the prevention of prostate cancer, but because the overall risk for high-grade tumors is still low (1% in the REDUCE trial), they remain appropriate when risks versus benefits are weighed in the treatment of BPH-related bladder retention. They are not, however, the chemopreventive solution that was hoped for.

For additional information regarding the FDA guidance and clinical trial results, visit www.fda.gov/Drugs/DrugSafety/ucm258314.htm.

NOTEWORTHY

Pancreatic Regimen Has Significant Trade-Offs

According to Conroy et al. (2011), a combination regimen including 5-fluorouracil (5-FU), oxaliplatin, irinotecan, and leucovorin (FOLFIRINOX) may offer significant survival advantage over single-agent gemcitabine (Gemzar®) in the treatment of metastatic pancreatic cancer, but the survival advantage should be weighed against the significant toxicities of FOLFIRINOX. In the French study comparing the two regimens (N = 342), FOLFIRINOX was associated with a median overall survival of 11.1 months compared to 6.8 months on gemcitabine ($p < 0.001$).

The gemcitabine arm received gemcitabine 1,000 mg/m^2 for seven of eight weeks and then weekly for four weeks. The FOLFINOX arm received oxaliplatin 85 mg/m^2, irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, and 5-FU 400 mg/m^2 bolus followed by a 46-hour infusion of 5-FU 2,400 mg/m^2 every two weeks. Chemotherapy continued for six months in those who responded to therapy.

Despite the increased toxicities associated with the aggressive FOLFIRINOX approach, such as febrile neutropenia (5.4%), fewer patients in the FOLFIRINOX arm (31%) reported decreased quality of life at six months compared to patients on gemcitabine (66%) ($p < 0.001$).

FOLFIRINOX is included in the National Comprehensive Cancer Network (NCCN) guidelines as a first-line treatment option for metastatic pancreatic cancer. Common toxicities include neutropenia (47%), fatigue (24%), vomiting (17%), nausea (16%), and diarrhea (12%) (NCCN, 2011). Nurses should educate patients regarding potential adverse effects and the use of supportive measures such as granulocyte–colony-stimulating factor for neutropenia that may help to minimize adverse events.

For NCCN guidelines, visit www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf.

Conroy, T., Desseigne, F., Ychou, M., Bouché, O., Guimbaud, R., Bécouarm, Y., . . . Ducreux, M. (2011). FOLIRINOX versus gemcitabine for metastatic pancreatic cancer. *New England Journal of Medicine, 364,* 1817–1825.

National Comprehensive Cancer Network. (2011). *NCCN Guidelines™: Pancreatic adenocarcinoma* [v.2.2011]. Retrieved from http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf

Thermograms Are Not Substitutes for Mammography

The FDA has issued a safety alert regarding the use of thermograms to detect breast cancer. Thermograms are images taken by an infrared camera that show patterns of heat and blood flow near the skin surface. The FDA's concern is that some manufacturer marketing strategies may lead patients to mistakenly believe that thermograms are a safer, possibly better, alternative to mammography for the detection of breast tumors. That is not the case, and although thermograms are marketed for the detection of many diseases (e.g., embolisms), the FDA has not approved thermograms for the screening of any medical condition when used alone. Patients who ask about thermography should be informed that mammograms, according to screening guidelines or as recommended by the healthcare provider, remain the screening method of choice. Patients who are concerned because of misinformation in thermogram promotional material about mammograms (e.g., the procedure can cause the spread of cancer through compression of the tumor) should be reassured and provided with accurate information.

For more information, and to view warning letters sent to manufacturers and practitioners of thermography, visit www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm257259.htm.

PRODUCT UPDATE

New Silicone-Based Tape Safer for Sensitive Skin

Adhesive tape-related skin injuries are common in patients with fragile skin. To minimize the risk for trauma, paper tapes frequently are used when medical tape is required, but they often provide less-than-optimal adhesiveness. 3M™ is marketing 3M Kind Removal Silicone Tape as an alternative to paper tape. The company asserts the product provides reliable adhesion via silicone-based technology that minimizes tissue trauma during removal.

For more information, visit http://solutions.3m.com/wps/portal/3M/en_US/3MSWC/Skin-Wound-Care/ProductDirectory/MedicalTapes/Silicone_Medical_Tapes?WT.mc_id=www.3M.com/SiliconeTape.

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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