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