PHARMACY CORNER

Everolimus Approved for Rare Pancreatic Cancer

The U.S. Food and Drug Administration (FDA) has approved everolimus (Afinitor®) to treat progressive neuroendocrine tumors (PNETs) located in the pancreas that are metastatic or unresectable. Approval was granted based on the results of the phase III RADIANT-3 trial in which patients (N = 410) were randomized to receive either everolimus 10 mg daily (n = 207) or placebo (n = 203). Progression-free survival was 11 months on treatment compared to 4.6 months on placebo ($p < 0.001$). Patients on placebo who showed signs of disease progression were allowed to change to everolimus, which 73% (n = 148) did.

The drug is not intended as curative treatment, but rather as a medication to slow the growth and spread of cancer. Common adverse events affecting 30% or more of patients with advanced PNET treated with everolimus included stomatitis, rash, diarrhea, fatigue, edema, abdominal pain, nausea, fever, and headache.

The normal dosing of 10 mg orally per day may need to be adjusted in patients with hepatic impairment or with concomitant use of CYP3A4 inducers or inhibitors. The pills should not be crushed and should be taken with a full glass of water. In patients who have difficulty swallowing, the pill can be dissolved by gently stirring into about 30 ml of water.

For additional information, visit www.pharma.us.novartis.com/product/pi/pdf/afinitor.pdf.

New Treatment Available for Resistant Prostate Cancer

The FDA has approved abiraterone acetate (Zytiga™) in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer in patients who have been treated previously with docetaxel (Taxotere®). Abiraterone acetate is an androgen biosynthesis inhibitor that works by reducing serum levels of testosterone and other androgens—affecting production of testicular androgens as well as production of androgens by the adrenals and tumor itself.

In a multicenter, placebo-controlled phase III clinical trial (N = 1,195), patients were randomized to receive abiraterone acetate 1,000 mg orally (n = 797) or placebo (n = 398). Both groups received prednisone 5 mg orally daily. All patients enrolled in the trial demonstrated advanced disease. Ninety percent of participants had metastatic bone disease and 30% had metastatic visceral disease. Patients in the treatment arm demonstrated a median survival of 15.8 months compared to 11.2 months in the placebo arm.

One possible limitation for generalizing trial results was racial distribution, as 93% of patients were Caucasian.

Adverse drug reactions occurring more frequently on abiraterone acetate compared to placebo included joint swelling or discomfort (30%), hypokalemia (28%), edema (27%), muscle discomfort (26%), low serum phosphorous (24%), hot flush (19%), diarrhea (18%), urinary tract infection (12%), cough (11%), hypertension (9%), arrhythmia (7%), urinary frequency (7%), nocturia (6%), dyspepsia (6%), and upper respiratory tract infection (5%).

Abiraterone acetate normally is dosed at 1,000 mg daily and given concomitantly with prednisone 5 mg orally BID. The drug must be taken on an empty stomach with no food two hours before or one hour following dosage administration. Taking the drug with food can cause an up to 10-fold exposure to the drug.

Dosage may require reduction in the presence of hepatic impairment.

For additional information, visit www.zytiga.com/pdf/prescribing_information.pdf#zoom=100.

Vandetanib Now Used for Medullary Thyroid Cancer

The FDA has approved vandetanib for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease.

Approval was granted based on the results of a double-blind randomized trial in which patients (N = 331) were randomized to receive vandetanib 300 mg daily orally (n = 231) or placebo (n = 100). At 30 months, vandetanib demonstrated superiority over placebo in progression-free survival (hazard ratio [HR] = 0.31; 95% confidence interval [CI] = 0.24–0.53; $p < 0.0001$). Patients on placebo were allowed to switch to open-labeled vandetanib on progression of disease. No complete responses were noted while on vandetanib, but 44% demonstrated partial responses compared to 1% in the placebo arm. No significant benefit was noted in overall survival.

Patients should be educated about the potentially serious adverse effects of vandetanib therapy. QT prolongation, torsades de pointes, and sudden death have been associated with the drug. Because the drug has a long half-life (19 days), adverse cardiac effects may be slow to resolve. Electrolyte abnormalities should be corrected before beginning therapy, and other medications known to prolong the QT interval should be avoided when possible. Electrocardiograms should be performed at baseline and routine intervals while on therapy.

Vandetamib is a tyrosine kinase inhibitor, therefore the common adverse reactions (affecting more than 20% of patients) of diarrhea or colitis (57%), rash (53%), and acneiform dermatitis (35%) are similar to other medications in this class of drugs. Additional adverse reactions include nausea (33%), hypertension (33%), headache (26%), fatigue (24%), decreased appetite (21%), and abdominal pain (21%). Common laboratory abnormalities include hypocalcemia and elevations in alanine aminotransferase. Although mild skin reactions are anticipated, severe reactions may necessitate cessation of therapy. As with other tyrosine kinase inhibitors, vandetanib has been associated with development of interstitial lung disease, and patients should be monitored appropriately.

Thyroid function should be monitored. In the trial, 90% of patients had a previous thyroidectomy. Of those patients, 49% required increased thyroid replacement therapy after starting vandetanib.

Usual dosing is 300 mg orally daily with reduction to 200 mg in the presence of renal impairment. Concomitant administration of strong CYP3A4 inducers should be avoided. Tablets should not be

crushed and contact with the skin should be avoided.

For additional information, visit www1.astrazeneca-us.com/pi/vandetanib.pdf.

NOTEWORTHY

Drug May Improve Smoking Cessation

As reported by Hajek, McRobbie, Myers, Stapleton, and Dhanji (2011), smoking cessation may improve by starting varenicline (Chantix®) earlier than the recommended one week prior to smoking cessation. In a randomized trial conducted in London, patients (N = 101) were randomized to receive four weeks of varenicline or three weeks of placebo followed by one week of varenicline prior to a planned smoking cessation date. Both groups were allowed to continue therapy up to 12 weeks after the planned smoking cessation date.

Although the additional weeks of therapy prior to cessation did not improve withdrawal symptoms compared to the placebo arm, improvement was noted in the percentage of patients who maintained abstinence at the end of 12 weeks (47% in the four-week treatment arm versus 21% in the three weeks of placebo followed by one week of treatment).

Although the study implies that increasing the preload time with varenicline can help smokers succeed in quitting, limitations of the study include the small sample size and the need for longer-term follow-up to determine whether the cessation advantage persists over time.

For package insert information with warnings and precautions during treatment with varenicline, visit http://media.pfizer.com/files/products/uspi_chantix.pdf.

Hajek, P., McRobbie, H.J., Myers, K.E., Stapleton, J., & Dhanji, A.R. (2011). Use of varenicline for 4 weeks before quitting smoking: Decrease in ad lib smoking and increase in smoking cessation rates. *Archives of Internal Medicine, 171*, 770–777. doi:10.1001/archinternmed.2011.138

Human Papillomavirus Not Associated With Lung Cancer

As reported by Koshiol et al. (2011), human papillomavirus (HPV) does not appear to be associated with lung cancer. HPV has been linked to oropharyngeal cancers and, based in part on anatomical proximity, HPV was hypothesized as a contributory factor in some occurrences of lung cancer. The researchers selected 450 patients with lung cancer from the population-based case-control Environment and Genetics in Lung Cancer Etiology study conducted in Italy. Of those, 399 patients had adequate tissue samples for HPV DNA detection assays. Using multiple tissue specimens from each patient, only two samples tested low-positive for HPV, and subsequent genotype-specific testing did not confirm the presence of HPV in these. Specimens were evaluated specifically for HPV 16 and HPV 18 subtypes, but some also were tested for as many as 54 HPV subtypes.

The researchers found fault with prior studies that seemed to link HPV to lung cancer, citing factors such as potential contamination of tissue specimens obtained and less advanced detection techniques.

Smoking is inarguably the primary contributing factor to lung cancer, but the study authors suggested a need to examine other potential contributing factors because most smokers do not develop lung cancer and many patients with lung cancer have never smoked. One weakness with that argument is that many smokers die of other causes, including those related to smoking. The absence of lung cancer does not prove the risk was not increased, nor that lung cancer may have occurred had the smoker lived longer.

Koshiol, J., Rotunno, M., Gillison, M.L., Van Doorn, L.J., Chaturvedi, A.K., Tarantini, L., . . . Caporaso, N.E. (2011). Assessment of human papillomavirus in lung tumor tissue. *Journal of the National Cancer Institute, 103*, 501–507.

PRODUCTS

Portable Device Treats Glioblastoma Multiforme

The FDA has granted approval with restrictions for the NovoTTF-100A System™, a device that, according to the manufacturer, kills tumor cells of patients with progressive or recurrent glioblastoma multiforme. The battery-operated device, via electrodes attached to the scalp, generates alternating electrical currents the manufacturer calls tumor treatment fields, which are believed to interfere with and cause cell death in the rapidly dividing cells of glioblastoma multiforme. Tumor treatment fields are not believed to have a significant effect on healthy brain cells that proliferate very slowly, if at all.

NovoTTF-100A is offered as an alternative to chemotherapy for patients who are at least 22 years old, have experienced recurrence in the supratentorial region of the brain, and have exhausted surgical and radiation therapy options. The device is intended as monotherapy.

In clinical trial data submitted to the FDA, patients received either therapy with the NovoTTF-100A (n = 120) or best standard chemotherapy (BSC) (n = 117). Patients on chemotherapy received widely varying regimens that included such agents as bevacizumab, carboplatin, nitrosureas, and erlotinib. Unfortunately, because of how the trial was designed, direct comparisons between NovoTTF-100A and individual chemotherapy regimens is not possible. However, NovoTTF-100A did show a comparable median overall survival, with NovoTTF-100A at 6.3 months and BSC at 6.4 months (HR = 1; 95% CI = 0.76–1.32; p = 0.98).

Although this treatment does not demonstrate a survival benefit and glioblastoma multiforme remains a disease with poor prognosis, suggested benefits of using the NovoTTF-100A include improved quality of life. Chemotherapy often is accompanied by unpleasant side effects and, according to NovoCure, treatment with the device has no serious adverse effects. Mild skin irritation at the contact points on the scalp were noted on trial, but that usually was relieved with topical steroids.

Use of the device requires being attached for at least 18 hours a day continuously, and the scalp must be shaved every two weeks. NovoCure suggests the use of a backpack or other bag to carry the device during daily routines. Treatment with NovoTTF-100A should last a minimum of four weeks.

For additional information, visit www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm254480.htm.

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.

Digital Object Identifier: 10.1188/11.ONF.485-486