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