PHARMACY CORNER

Sunitinib Successful in Pancreatic Cancer Trial

As reported by Raymond et al. (2011), the small molecule drug sunitinib malate (Sutent®, Pfizer, Inc.) may have utility in treating neuroendocrine pancreatic cancer. In a multicenter, randomized, placebo-controlled phase III clinical trial (N = 171), researchers compared oral sunitinib 37.5 mg to best supportive care in patients with well-differentiated, advanced neuroendocrine pancreatic tumors. Compared to placebo, sunitinib demonstrated superiority in median progression-free survival and objective response rate. Patients in the sunitinib arm demonstrated a median progression-free survival of 11.4 months versus 5.5 months on placebo ($p < 0.001$). A 9.3% objective response rate was seen with sunitinib, but none with placebo. The study was ended early because of the clear advantage seen on treatment. At the end of the study, 10% of patients in the sunitinib arm had died compared to 25% in the placebo arm ($p = 0.02$).

Sunitinib is a multiple tyrosine kinase inhibitor that restricts the activity of platelet-derived growth factor receptors, vascular endothelial growth factor receptors, stem cell factor receptors, and others. Through inhibition of the tyrosine kinase pathway, the drug slows tumor growth and metastasis. The drug has been approved by the U.S. Food and Drug Administration for use in the treatment of gastrointestinal stromal tumors after progression on or intolerance to imatinib mesylate (Gleevec®, Novartis Pharmaceuticals) and in the treatment of advanced renal cell carcinoma.

Common side effects experienced with sunitinib are diarrhea, nausea, vomiting, asthenia (weakness), rash, hair color changes, and fatigue. Severe hepatotoxicity has been observed in patients on therapy, and laboratory values should be monitored appropriately.

For additional precautions, visit www.pfizerpro.com/hcp/oncology/sutent/indication?rid=/wyeth_html/home/minisites/oncology/sutent/pi/boxed-warning.html.

Raymond, E., Dahan, L., Raoul, J.L., Bang, Y.J., Borbath, I., Lombard-Bohas, C., . . . Ruszniewski, P. (2011). Sunitinib malate for the treatment of pancreatic neuroendocrine tumors. *New England Journal of Medicine, 364,* 501–513. doi: 10.1056/NEJMoa1003825

SAFETY CONCERNS

Bevacizumab Increases Risk of Fatal Adverse Effects

The addition of bevacizumab (Avastin®, Genentech) to chemotherapy or other biologic therapies is associated with an increased risk for fatal adverse events. A meta-analysis of 16 randomized, controlled trials with 10,217 participants showed that bevacizumab was associated with a 2.5% incidence of fatal adverse effects compared to 1.7% incidence in the control arms (Ranpura, Hapani, & Wu, 2011). The most common causes of mortality were hemorrhage (23.5%), neutropenia (12.2%), and gastrointestinal perforation (7.1%).

The mortality risk appears to increase based on the drugs given with bevacizumab. Most notably, taxanes and platinum agents were associated with dramatic increases in the risk for fatal adverse effects (relative risk = 3.49; confidence interval = 1.82–6.66).

Bevacizumab is a monoclonal antibody that binds to the ligand vascular endothelial growth factor and works by inhibiting the development of new blood vessels. Tumors cannot survive without adequate oxygenation delivered via new blood vessels.

Ranpura, V., Hapani, S., & Wu, S. (2011). Treatment-related mortality with bevacizumab in cancer patients: A meta-analysis. *JAMA, 305,* 487–494. doi: 10.1001/jama.2011.51

NOTEWORTHY

Lights Out to Reduce Breast Cancer Risk

Working the night shift previously had been linked to an increased risk of breast cancer in women, but even sleeping with the lights on may be associated with a greater incidence of cancer. Light exposure during sleep hours has been associated with a 22% increased risk for breast cancer ($p < 0.001$) in a case-controlled study of northern Israeli women (N = 1,679: 794 with breast cancer and 885 controls) (Kloog, Portnov, Rennert, & Haim, 2011). Data were extracted from the Breast Cancer in Northern Israel Study, started in 2000, which sought to identify molecular and environmental contributors to breast cancer. Light intensity, defined in a range from completely dark to very strong light (i.e., with all light switches turned on), emerged as a strong predictor of cancer risk, with higher intensity associated with higher incidence. Religion also emerged as a predictor of cancer risk, but that is believed to be associated with the differing birth rates among Jewish women compared to Arab women participating in the study.

The exact reason for the association between artificial light and breast cancer is not known, but hypothesized mechanisms include disruptions in melatonin production and effects on circadian rhythms.

Kloog, I., Portnov, B.A., Rennert, H.S., & Haim, A. (2011). Does the modern urbanized sleeping habitat pose a breast cancer risk? *Chronobiology International, 28,* 76–80. doi: 10.3109/07420528.2010.531490

Cost of Cancer Care Expected to Increase Dramatically by 2020

Although the overall incidence of cancer is declining and the length of survival is increasing, the projected costs for cancer care in the United States are anticipated to increase dramatically by the year 2020 compared to 2010, based on changes in the population and current trends (Mariotto, Yabroff, Shao, Feuer, & Brown, 2011). The annual cost for treating cancer may reach $173 billion by 2020 (in 2010 dollars), which represents an increase of 39%. The greatest increases in expense are expected to be seen in the treatment and care of patients with prostate or breast cancer, which remain the most common forms of cancer for men and women, respectively, in the United States.

Mariotto, A.B., Yabroff, K.R., Shao, Y., Feuer, E.J., & Brown, M.L. (2011). Projections of the cost of cancer care in the