PHARMACY CORNER

New Prostate Cancer Therapy Helps Body Attack Cancer Cells

The U.S. Food and Drug Administration (FDA) has approved sipuleucel-T (Provenge®, Dendreon Corp.) for the treatment of asymptomatic or minimally symptomatic metastatic prostate cancer that is castrate resistant (hormone refractory).

Provenge, sometimes referred to as a vaccine, works by stimulating a patient's own immune system to attack the cancer cells. Patients typically receive three doses of Provenge, an autologous immune therapy, in approximately two-week intervals. Doses are prepared by first acquiring the patient's own immune cells (CD54+ cells) through leukapheresis three days prior to the planned dose administration. In the laboratory, these immune cells are then exposed to a molecule commonly found in prostate cancers (prostatic acid phosphatase)—essentially "priming" the immune cells to recognize prostate cancer cells as cells requiring destruction. These prepared immune cells are then given back to the patient via IV administration.

FDA approval for Provenge was largely based on results of the phase III IMPACT trial, a randomized, double-blind, placebo-controlled trial (N = 512) in which patients treated with Provenge (n = 341) experienced an increased overall survival of 4.1 months compared to placebo (n = 171). Patients on treatment experienced a median survival of 25.8 months versus 21.7 months on placebo (p = 0.032, hazard ratio [HR] = 0.775, 95% confidence interval [CI] = 0.614, 0.979, respectively). Common adverse reactions to Provenge included chills, fever, back pain, nausea, joint pain, and headaches. Serious adverse reactions seen more commonly with Provenge compared to placebo in the IMPACT trial as well as prior smaller studies included both hemorrhagic and ischemic strokes (3.5% versus 2.6% on placebo).

Infusion reactions were common (71.2%), but serious grade 3 reactions were only seen in 3.5% of patients receiving Provenge. Patients should be given acetaminophen and an oral antihistamine such as diphenhydramine prior to infusions to minimize reactions, and Provenge should be given over approximately 60 minutes without the use of cell filters. If infusion reactions occur, the rate of infusion should be slowed or, in the case of severe reactions, stopped.

For additional information, visit www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm210174.htm.

Bevacizumab Use May Increase Survival in Renal Cell Carcinoma

As reported by Rini et al. (2010), the addition of bevacizumab (Avastin®, Genentech) to interferon-α (IFN-α) therapy may improve overall survival in renal cell carcinoma. A phase III randomized trial involving patients with metastatic clear cell renal cell carcinoma (N = 732) compared standard IFN-α therapy to IFN-α plus bevacizumab 10 mg/kg every two weeks. Modest improvements in overall survival were seen in the IFN-α plus bevacizumab arm (18.3 months, 95% CI = 16.5–22.5 months) compared to IFN-α monotherapy (17.4 months, 95% CI = 14.4–20 months; p = 0.069). Not surprisingly, the bevacizumab arm experienced greater incidence of grades 3 and 4 hypertension. Interestingly, the experience of hypertension after initiating bevacizumab was correlated with greater progression-free survival and overall survival—indicating that hypertension may be a useful indirect indicator of response to therapy.

Rini, B.I., Halabi, S., Rosenberg, J.E., Stadler, W.M., Vaena, D.A., Archer, L., . . . Small, E.J. (2010). Phase III trial of bevacizumab plus interferon alpha versus interferon alfa monotherapy in patients with metastatic renal cell carcinoma: Final results of CALGB 90206. *Journal of Clinical Oncology, 28*, 2137–2143. doi: 10.1200/JCO.2009.26.5561

Erlotinib Gains Expanded Role in Non-Small Cell Lung Cancer

Erlotinib (Tarceva®, Genentech), an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), has received FDA approval for use as maintenance therapy for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose disease has not progressed after four cycles of standard first-line platinum-based chemotherapy. Prior approvals had been granted for erlotinib usage in patients with NSCLC following the failure of standard chemotherapy.

Approval as maintenance therapy in NSCLC was granted based on a phase III randomized, double-blind, placebo-controlled study (N = 889, n = 438 in the erlotinib arm, n = 451 in the placebo arm) which demonstrated the efficacy and safety of erlotinib in this population. Modest gains were seen in overall survival in the treatment arm versus placebo (12 months versus 11 months, p = 0.0088, HR = 0.81, 95% CI = 0.7, 0.95, respectively).

Maintenance dosing of erlotinib in NSCLC is 150 mg per day taken at least one hour before food or two hours after food, but dosages may require reduction if severe adverse reactions occur. The most common adverse effects with erlotinib are dermatologic reactions (acneiform rash) and diarrhea. Diarrhea is typically easily managed with loperamide, but patients should be educated regarding notifying the healthcare team when diarrhea persists. Patients also should be educated to anticipate dermatologic reactions and to avoid sunlight as this may worsen the condition.

For additional information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2010/021743s14s16lbl.pdf.

SAFETY CONCERNS

Gonadotropin-Releasing Hormone Drugs May Pose Risks

The FDA is currently evaluating whether gonadotropin-releasing hormone (GnRH) agonist drugs, used in the treatment of prostate cancer, lead to an increased risk of diabetes and cardiac toxicities. According to the FDA, in six studies of men being treated with these androgen-deprivation agents for prostate cancer, small increases in the incidence of diabetes and cardiovascular events (i.e., heart attacks, sudden cardiac death, and stroke) were observed. However, a specific causal relationship has not been identified. The FDA suggests that patients undergoing GnRH therapy for prostate cancer be closely monitored for