the groups that received only chemotherapy, indicating no significant deterioration in quality of life.

BEV represents the first targeted agent that improves the outcome of metastatic or relapsed cervical cancer when added to an established chemotherapy regimen.

Sorafenib Delays Progression of Treatment-Resistant Differentiated Thyroid Cancer

Written by Wayne Kuznar

The multitargeted agent sorafenib is the first therapy that has shown promise in a Phase 3 trial to extend progression-free survival (PFS) in patients with metastatic differentiated thyroid cancer that is refractory to standard radioactive iodine (RAI) therapy.

Interim results from a double-blind, placebo-controlled randomized Phase 3 Study of Sorafenib in Locally Advanced or Metastatic Patients With Radioactive Iodine Refractory Thyroid Cancer [DECISION; NCT00984282; Brose MS et al. *J Clin Oncol* 2013 (suppl; abstr 4)], for the treatment of patients with RAI refractory differentiated thyroid cancer were presented by Marcia S. Brose, MD, PhD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Differentiated thyroid cancer accounts for the majority of the >60,000 thyroid cancer cases diagnosed each year in the United States [Howlader N et al. *SEER Cancer Statistics Review.* http://seer.cancer.gov/statfacts/html/thyro.html. Accessed June 2013]. Although cure rates of differentiated thyroid cancer are generally high following standard treatment with surgery and RAI, the disease becomes refractory to RAI in ~15% of patients [Pacini F et al. *Expert Rev Endocrinol Metab* 2012; Xing M et al. *Lancet* 2013]. Their median survival after resistance develops is 2.5 to 3.5 years, and bone, pulmonary, and brain complications occur frequently [Durante C et al. *J Clin Endocrinol Metab* 2006; Robbins RJ et al. *J Clin Endocrinol Metab* 2006]. There is no standard therapy for patients with RAI-refractory differentiated thyroid cancer, with palliative care being the main option.

Sorafenib is a multikinase inhibitor with activity against RAF kinase and several receptor tyrosine kinases, including vascular endothelial growth factor receptor 1 to 3, platelet-derived growth factor receptors, BRAF, RET, and c-KIT.

In DECISION, 417 patients with locally advanced or metastatic, RAI-resistant differentiated thyroid cancer whose disease had progressed within the preceding 14 months (as defined by RECIST 1.0 criteria) were randomly assigned in a 1:1 ratio to receive sorafenib 400 mg orally BID or placebo. Allowance was made for crossover from placebo to sorafenib upon disease progression. The study was conducted in 89 centers across North America, Europe, and Asia.

The median PFS by independent central review, the primary endpoint, was 10.8 months in the sorafenib group versus 5.8 months in the placebo arm (HR, 0.587; p<0.0001). The benefit with sorafenib on PFS was consistent across subgroups examined. At disease progression, 150 patients assigned to placebo (71%) and 55 assigned to sorafenib (27%) received open-label sorafenib. The median overall survival has not been reached in either group.

The response rates were 12.2% and 0.5% in the sorafenib and placebo arms, respectively (p<0.0001). All were partial responses; no complete responses were observed.

Dose modification due to adverse events (AEs) was necessary in 77.8% of the sorafenib arm and 30.1% of the placebo arm. Discontinuation due to AEs occurred in 18.8% of sorafenib-treated patients versus 3.8% of the placebo group. Tolerability was consistent with the known sorafenib safety profile. The most common any-grade treatment-emergent AEs in the sorafenib arm were hand-foot skin reaction, diarrhea, alopecia, rash/desquamation, fatigue, weight loss, and hypertension. There was one death in each arm that was attributed to the study drug.

Sorafenib significantly improved PFS and extended median PFS by 5 months compared with placebo in RAI-refractory differentiated thyroid cancer, representing the first effective agent in this a rare cancer with poor prognosis and no established treatment to date.

Tamoxifen in Estrogen Receptor-Positive Breast Cancer: 10 Years Superior to 5 Years

Written by Wayne Kuznar

Ten years of adjuvant tamoxifen is superior to 5 years in reducing the rates of late recurrence and death in women with estrogen receptor (ER)-positive breast cancer.

Breast cancer mortality is reduced by about one third over 15 years when women with ER-positive tumors are treated with 5 years of adjuvant tamoxifen. The effect of an additional 5 years of treatment on breast cancer recurrence and death was examined in the randomized Phase 3 Adjuvant Tamoxifen: To Offer More? study [aTTom; ISRCTN17222211; Gray RG et al. *J Clin Oncol* 2013 (suppl; abstr 5)], which was presented by Richard G. Gray, MSc, University of Oxford, Oxford, United Kingdom.

In aTTom, 6953 women in the United Kingdom who had been taking tamoxifen for 5 years were randomized to continuing treatment for an additional 5 years or stopping treatment. During the 15-year enrollment period, ER status was tested in only ~40% of the women; ER status in the remaining 60% was unknown. About 75% of the women assigned to continue tamoxifen had continued taking it for the 5 extra years.