HEM/ONC News

By Stacey Small

Bevacizumab Significantly Improves Survival in Patients With Recurrent Cervical Cancer

According to a planned interim analysis of the Gynecologic Oncology Group (GOG) 240 study, bevacizumab (Avastin; Genentech, A Member of the Roche Group) significantly improved overall survival when added to chemotherapy in patients with recurrent/persistent or metastatic cervical cancer. Tewari and associates presented their findings at the 2013 American Society of Clinical Oncology (ASCO) annual meeting (Abstract 3). Patients were assigned to 1 of 4 treatment arms: cisplatin plus paclitaxel (the current standard of care), topotecan plus paclitaxel, or the same 2 regimens with bevacizumab added. Treatment cycles were repeated every 21 days until disease progression, unacceptable toxicity, or complete response. The groups were well matched for age, histology, race, disease stage, and performance status. There was a statistically significant difference in overall survival. Patients who received bevacizumab lived for a median of 3.7 months longer than patients who did not receive bevacizumab. The median overall survival was 17 months with bevacizumab and 13.3 months without it (hazard ratio [HR] of death, 0.71; 97.6% confidence interval [CI], 0.54–0.94; *P*=.0035). Furthermore, the addition of bevacizumab produced significantly better response rates (48% vs 36%; *P*=.00807), as well as improved progression-free survival (PFS; 8.2 months vs 5.9 months; *P*=.0002). The addition of bevacizumab to chemotherapy led to more adverse effects, including grade 3/4 bleeding (5% vs 1%), thrombosis/embolism (9% vs 2%), and gastrointestinal fistula (3% vs 0%). However, such adverse effects were consistent with the known profile of bevacizumab. Results of this trial were submitted to the US Food and Drug Administration (FDA) to support the approval of bevacizumab for the new indication of advanced cervical cancer.

PD-L1 Antibody Induces Durable Responses in Patients With Renal Cell Carcinoma

Durable responses were observed in patients with renal cell carcinoma who were treated with the PD-L1 antibody MPDL3280A. Presented by Cho and colleagues at the 2013 ASCO annual meeting (Abstract 4505), this immunotherapy trial was one of few that enrolled patients with non-clear cell histologies; some clinical activity was observed in these patients. As part of a larger dose escalation and dose expansion study, 53 patients with renal cell carcinoma received intravenous MPDL3280A 3 times per week at doses of 10 mg/kg, 15 mg/kg, or 20 mg/kg. Among the renal cell carcinoma patients, 87% had clear cell carcinoma, 7% had papillary carcinoma, and 4% had sarcomatoid histologies. No maximum tolerated dose, dose-limiting toxicities, or treatment-related deaths were observed among renal cell carcinoma patients. Of the 140 patients in the total population who were evaluable for efficacy, the overall response rate (ORR) was 21% (24-week PFS, 45%), with the highest number of therapy responses occurring in patients with lung cancer (n=41; ORR 22%; 24-week PFS, 46%), melanoma (n=38; ORR 29%; 24-week PFS, 43%), and renal cell carcinoma (n=47; ORR 13%; 24-week PFS, 53%). Treatment responses are ongoing.

Idelalisib Plus Rituximab Produces High Responses and Durable Disease Control in Treatment-Naïve CLL Patients

Combination therapy with idelalisib (GS-1101, Gilead Sciences) and rituximab (Rituxan, Genentech/Biogen Idec) yielded an ORR of 97% in a cohort of 64 older (≥65 years), treatment-naïve patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma, according to results of a phase II study presented by O'Brien at the 2013 ASCO annual meeting (Abstract 7005). Patients were given idelalisib 150 mg twice daily for 48 weeks and rituximab 375 mg/m^2 once weekly for 8 weeks. Complete responses occurred in 19% of patients and partial responses occurred in 78%. The 9 patients with chromosome 17p deletion (del 17p; n=6) or *TP53* mutation (n=3)—which have been linked to poor prognosis—all responded to therapy, including 3 patients with a complete response. PFS at 24 months was 93% among all patients, and 100% among patients with *TP53* mutation or del 17p. Patients who completed 48 weeks of therapy without progression were allowed to stay on treatment in an extension study. Forty-three patients completed 48 weeks of treatment. There were 21 patients who discontinued treatment owing to adverse events (n=17), death (n=3), or withdrawal of consent (n=1). Of the 40 patients who entered the extension study, 33 remained on treatment as of May 2013. During the primary and extension study, grade 3 diarrhea and/or colitis was reported in 23% of patients, grade 3 or greater pneumonia in 17%, transaminase elevations in 23%, and neutropenia in 28%. Based on these data, researchers are evaluating phase III study designs for idelalisib as part of a frontline treatment regimen in CLL.