HEM/ONC News

By Devon Schuyler

Termination Recommended for Phase 3 Trial of Onartuzumab in NSCLC

An independent data monitoring committee has recommended that a phase 3 study of onartuzumab for non–small cell lung cancer (NSCLC) be halted owing to a "lack of clinically meaningful efficacy," according to Genentech, the drug's developer.

The phase 3 study, called METLung, includes 499 patients with advanced, second- or third-line NSCLC identified as MET-positive by immunochemistry. All patients were randomly assigned to receive erlotinib (Tarceva, Genentech/Astellas) 150 mg daily by mouth in addition to either intravenous onartuzumab (also known as MetMAb) 15 mg/kg or an intravenous placebo every 3 weeks. The primary endpoint of the study is overall survival (OS); secondary endpoints include progression-free survival (PFS), response rate, and safety profile.

At a prespecified interim analysis, the rate of adverse events was similar between the 2 arms, and combination treatment with onartuzumab and erlotinib was not more efficacious than erlotinib alone.

Onartuzumab is an investigational monovalent monoclonal antibody that is designed specifically to target the MET receptor. It is being studied for use in a variety of cancers.

Circulating Tumor Cells Predict Prognosis in Metastatic Breast Cancer

The use of circulating tumor cell (CTC) count has prognostic value in women with metastatic breast cancer, according to a study published online in *Lancet Oncology* on March 11. This pooled analysis study confirmed the findings of previous research on CTCs.

François-Clément Bidard and colleagues obtained records from 17 European centers on 911 patients with metastatic breast cancer who had received baseline CTC testing (CellSearch, Janssen Diagnostics). They found that 47% of the patients had a high CTC count (defined as at least 5 per 7.5 mL), and that these patients had decreased PFS (hazard ratio [HR], 1.92; 95% CI, 1.73-2.14; $P<.0001$) and OS (HR, 2.78; 95% CI, 2.42-3.19; $P<.0001$) compared with those who had a low CTC count (defined as less than 5 per 7.5 mL). CTC counts 3 to 5 weeks and 6 to 8 weeks after the start of treatment were associated with PFS and OS. CTC count was better at predicting prognosis than standard mucin-based serum biomarkers.

"These results confirm that CTCs are a powerful instrument for the personalised management of metastatic breast cancer, have strong clinical value, and are without major limits or contraindications," wrote Massimo Cristofanilli in an accompanying comment. He pointed out that patients with a low CTC count are likely to benefit from standard treatment, whereas those with a high CTC count might derive little benefit from these treatments. He recommended that CTC counts be considered for incorporation into the design of future clinical trials.

Bevacizumab Boosts PFS in Platinum-Resistant Ovarian Cancer

The addition of bevacizumab (Avastin, Genentech) to single-agent chemotherapy for platinum-resistant ovarian cancer led to statistically significant improvements in PFS and objective response rate (ORR) but not in OS, according to a phase 3 trial led by Eric Pujade-Lauraine that was published online March 17 in the *Journal of Clinical Oncology*.

The trial, called AURELIA (A Study of Avastin [Bevacizumab] Added to Chemotherapy in Patients With Platinum-Resistant Ovarian Cancer), involved 361 patients with ovarian cancer that had progressed within 6 months after completing platinum-based chemotherapy. Patients were randomly assigned to receive chemotherapy (either liposomal doxorubicin [Doxil, Janssen], paclitaxel, or topotecan) with or without bevacizumab.

Compared with chemotherapy alone, the addition of bevacizumab to chemotherapy significantly improved PFS from 3.4 to 6.7 months (HR, 0.48; 95% CI, 0.38-0.60; $P<.001$) and ORR from 11.8% to 27.3% ($P=.001$). Median OS was 16.6 months with chemotherapy alone and 16.6 months with bevacizumab plus chemotherapy, a difference that was not statistically significant. Hypertension of grade 2 or higher and proteinuria were more common with bevacizumab than without, and 2.2% of the bevacizumab-treated patients experienced gastrointestinal perforation.

In an editorial that accompanied the study, Joyce Liu and Stephen Cannistra wrote that the results of AURELIA support the use of bevacizumab plus chemotherapy in women with recurrent ovarian cancer, especially if they have symptomatic, platinum-resistant disease.

Bevacizumab does not have approval from the US Food and Drug Administration for any indication in ovarian cancer.