HEM/ONC News

By Stacey Small

Trastuzumab in HER2-Positive Lobular Breast Cancer: Results From the HERA Trial

In an article published in the April 15 online issue of the *Journal of Clinical Oncology*, Metzger-Filho and associates analyzed data from the HERA (Herceptin Adjuvant) trial to ascertain the magnitude of benefit of trastuzumab (Herceptin, Genentech) in patients with human epidermal growth factor receptor 2 (HER2)-positive invasive lobular carcinoma (ILC). Their analysis included patients randomized to receive 1 year of trastuzumab or observation (n=3,401). There were 187 patients with ILC and 3,213 patients with invasive ductal carcinoma (IDC) for comparison. Allred scores for estrogen receptor (ER), progesterone receptor (PgR), and HER2 copy number were compared for those tumors with central assessment of these parameters. ILC tumors were more likely to have high Allred scores than IDC tumors for both ER (36.9% vs 22.7%) and PgR (44.1% vs 28.5%). Low Allred scores were more common in IDC tumors. Patients with ILC tended to have lower HER2 copy numbers than IDC patients (35.7% vs 22.7%, respectively). In addition, the pattern of sites of first occurrence of a disease-free survival (DFS) event and the pattern of sites of first distant recurrence were similar for both ILC and IDC. At a median follow-up of 4 years, there did not appear to be a difference in magnitude of trastuzumab benefit in the IDC and ILC subgroups. The hazard ratio (HR) for DFS comparing 1 year of trastuzumab with observation was 0.63 for ILC (95% confidence interval [CI], 0.34–1.15) and 0.77 for IDC (95% CI, 0.67–0.89; *P*=.49 for interaction). For overall survival, the HR was 0.60 for ILC (95% CI, 0.27–1.31) and 0.86 for IDC (95% CI, 0.71–1.06; *P*=.29 for interaction). The researchers concluded that HER2-positive ILC patients will derive the same magnitude of benefit from trastuzumab as patients with HER2-positive IDC.

Inhibition of Tumor Metastasis: Preclinical Studies of Eribulin Mesylate

At the American Association for Cancer Research (AACR) 104th Annual Meeting in Washington, DC, preclinical research findings suggested that a potential novel mechanism of action for eribulin mesylate (Halaven, Eisai Co., Ltd) may be an inhibitory effect on tumor metastasis. In gene expression profiling (GEP) analyses of multiple cancer cell lines, eribulin was shown to alter expression in epithelial-mesenchymal transition (EMT) gene sets (abstract 1522). Dezso and colleagues sought to determine whether selective signal pathways were associated with eribulin activity compared to paclitaxel. Their comparison was based on GEP using 3 cancer cell line panels in vitro. Several tubulins were found to have significantly lower expression in cell lines treated with eribulin compared to paclitaxel, regardless of cancer panels. Pathways specific to cancer types were also identified. EMT was enriched in genes with significantly altered expression between eribulin and paclitaxel for breast cancer (*P*=3.4e-07) and endometrial cancer (*P*=.001), but not for ovarian cancer. EMT pathway gene expression was associated with eribulin sensitivity in breast cancer (*P*=.1) and paclitaxel sensitivity in endometrial cancer (*P*=.07). The investigators also found that selective signaling pathways were associated with drug sensitivity in breast cancer panels among clustered 394 pathways based on GEP. Another presentation by McCracken and coworkers (abstract 4502), which involved human breast xenograft tumors in rats, suggested that eribulin may prevent hypoxia in the tumor core by improving blood perfusion, thereby working to inhibit tumor metastasis.

Driver Mutations in NSCLC May Carry On From Primary to Metastatic Tumors

In the April 29 online issue of the *Journal of Clinical Oncology*, Soria and associates reported that more than 90% of non–small cell lung cancer (NSCLC) metastases shared genomic alterations with the primary tumor in a small clinical study. They examined the concordance in somatic mutations between archived tissue specimens of NSCLC and specimens obtained from metastatic lesions at recurrence in the same patients. A targeted next-generation sequencing assay was used to analyze primary and matched metastatic tumor pairs from 15 patients. No targeted therapy was administered to patients prior to biopsy of metastatic lesions. Only matched primary and metastatic tissue specimens with more than 50% cellularity were included. Comparison of recurrent alterations between primary and metastatic tumors showed a concordance of 94%, compared with 63% for presumed passenger alterations, which accounted for 80% of all mutations.