

NOAH Trial Shows Survival Benefit With Neoadjuvant Trastuzumab

In a phase III, international, open-label trial (Neoadjuvant Herceptin, NOAH), women with HER2-positive locally advanced or inflammatory breast cancer who received trastuzumab (Herceptin, Genentech) as neoadjuvant and adjuvant therapy had a significantly greater event-free survival (EFS) at 3 years. The study, which was published in the January 30 issue of *Lancet*, enrolled 235 patients who received either neoadjuvant trastuzumab plus a neoadjuvant chemotherapy regimen (doxorubicin, paclitaxel, cyclophosphamide, methotrexate and fluorouracil [5-FU]) followed by adjuvant trastuzumab or neoadjuvant chemotherapy alone. The primary endpoint was EFS, and the secondary endpoint was pathologic complete response. After a median follow-up of 3.2 years, 71% of women who received trastuzumab and 56% of women who received chemotherapy alone were event free. This difference resulted in a 41% reduction in the risk of recurrence (hazard ratio, 0.59; $P=.013$). Pathologic response was also higher in patients receiving trastuzumab compared to those receiving chemotherapy alone (38.5% vs 19.5%). Conversely, overall survival (OS) was not different between the 2 groups (87% with trastuzumab vs 79% with chemotherapy). In all the subgroups that were tested, particularly in those with inflammatory disease, trastuzumab administration produced a survival benefit. A safety analysis demonstrated a similar incidence of adverse events in both groups, and symptomatic heart failure was lower in patients receiving trastuzumab.

XELOX Improves Disease-free Survival in Elderly Stage III Colorectal Cancer Patients

According to a study (Abstract 284) reported by Dr. Haller and colleagues at the American Society of Clinical Oncology's annual Gastrointestinal Cancers Symposium, a combination of capecitabine and oxaliplatin (XELOX) improved disease-free survival (DFS) in patients with stage III colorectal cancer irrespective of age. The study (NO16968) examined 1,886 high-risk lymph node-positive patients randomized to either adjuvant XELOX or standard treatment of 5-FU and leucovorin (5-FU/LV). Study findings demonstrated a higher DFS rate in patients receiving XELOX compared with those receiving standard therapy at 3 (71% vs 67%), 4 (68.4% vs 62.3%), and 5 (66.1% vs 59.8%) years. An analysis of patients younger than

70 years as well as those 70 years or older also showed a survival benefit with XELOX. Based on these findings, it is evident that XELOX therapy can be considered for patients regardless of age.

Pazopanib Slows Progression of Advanced Kidney Cancer

Results from the phase III study that led to the approval of pazopanib (Votrient, GlaxoSmithKline) by the U.S. Food and Drug Administration were reported in the January 25 issue of *Journal of Clinical Oncology*. Investigators found that pazopanib slows disease progression by 54% in patients with advanced renal cell carcinoma (RCC). Pazopanib is an oral multi-targeted tyrosine kinase inhibitor that binds to the vascular endothelial growth factor receptor, the platelet-derived growth factor receptor, and the c-Kit receptor. The study enrolled 233 patients with previously untreated, locally advanced or metastatic RCC and 202 patients with RCC that had been previously treated with cytokine therapy (interferon or interleukin). Of all patients, 290 were assigned to pazopanib therapy and 145 to placebo. The progression-free survival (PFS) was significantly longer in patients receiving pazopanib compared to those receiving placebo (9.2 vs 4.2 months). This difference in PFS was particularly evident in patients with previously untreated RCC (11.1 months for pazopanib vs 2.8 months for placebo). In patients who were previously treated with cytokine therapy, those receiving pazopanib also demonstrated a PFS benefit (7.4 vs 4.2 months). OS data will be evaluated at follow-up. Diarrhea, hypertension, hair color changes, nausea, weight loss, and vomiting were among the most frequently reported adverse events.

FDA Approves Lapatinib/Letrozole Combination

On January 29, the FDA approved lapatinib (Tykerb, GlaxoSmithKline) in combination with letrozole (Femara, Novartis) for the treatment of postmenopausal women with hormone receptor-positive and HER2-positive advanced breast cancer for whom hormonal therapy is indicated. The approval was based on a study that demonstrated a significantly longer progression-free survival in women receiving the combination of lapatinib and letrozole compared to those receiving letrozole alone (34.5 vs 13 weeks). The most common adverse events reported with the combination therapy were diarrhea, rash, nausea, and fatigue.