The results of the PHARE trial were inconclusive for the noninferiority hypothesis. Nevertheless, a trend favoring the standard 12 months of treatment in DFS and OS was observed.

Breast Cancer: Updated Overall Survival Results from EMILIA

Written by ***Phil Vinall***

Trastuzumab emtansine (T-DM1) is a human epidermal growth factor receptor 2 (HER2)-targeted antibody-drug conjugate, composed of trastuzumab, a stable thioether linker, and the potent cytotoxic, microtubule inhibitor DM1. It retains the HER2-directed antitumor properties of trastuzumab and allows for the intracellular delivery of T-DM1 [LoRusso PM et al. *Clin Cancer Res* 2011]. Preclinical studies have shown T-DM1 to be up to 500 times more potent than taxane. Sunil Verma, MD, Sunnybrook Odette Cancer Center, Toronto, Ontario, Canada, reported updated study results of a trial showing that progression-free survival (PFS) and overall survival (OS) significantly improved in patients with breast cancer treated with T-DM1 compared with capecitabine (CAP) plus lapatinib (LAP). The study was published to coincide with the presentation [Verma S et al. *N Engl J Med* 2012].

An Open-Label Study of Trastuzumab Emtansine versus Capecitabine+Lapatinib in Patients with HER2-Positive Locally Advanced or Metastatic Breast Cancer [EMILIA; NCT00829166] was a randomized Phase 3 trial evaluating T-DM1 compared with CAP plus LAP. Patients with HER2-positive locally advanced or metastatic breast cancer, previously treated with taxane and trastuzumab were randomized to intravenous T-DM1 (3.6 mg/kg every 3 weeks; n=495) or oral CAP (1000 mg/m^2 BID on Days 1 to 14 every 3 weeks plus oral LAP 1250 mg QD on Days 1 to 21; n=496). The primary study end points were PFS, OS, and safety.

Subjects were a median age of 53 years, mostly White, and had an Eastern Cooperative Oncology Group Performance Status score of 0 (61% to 64%) or 1 (36% to 39%). Up to 80% of patients had measurable disease; up to 68% had visceral disease, and up to 33% had at least 3 sites of metastatic disease. About 55% of patients were estrogen and/or progesterone (ER/PR)-positive.

The final PFS and first interim OS analyses were presented at the 2012 annual American Society of Clinical Oncology meeting [Blackwell KL et al. ASCO 2012. Abstract LBA1]. The first interim OS analysis (median OS: CAP plus LAP, 23.3 months; T-DM1 not reached; HR, 0.621; 95% CI, 0.48 to 0.81; p=0.0005) did not cross the efficacy stopping boundary (p=0.0003 or HR=0.617). Dr. Verma presented results of a second interim analysis conducted after 52% of the total targeted number of OS events had been reached. In this analysis, OS significantly favored T-DM1 (30.9 vs 25.1 months; p=0.0006); median follow-up was 19.1 months for T-DM1 and 18.6 months for CAP plus LAP. The OS benefit was observed in most subgroups, including line of metastatic therapy (1st, 2nd, 3rd, or later), ER/PR status, and age, although the subgroup of patients aged >75 years was too small to confirm benefit. The secondary endpoints of objective response rate and duration of response also favored T-DM1.

Approximately 53% of CAP patients and 27% of LAP patients required a dose reduction compared with 16% of T-DM1 patients. T-DM1 was well tolerated and associated with fewer grade ≥3 adverse events (40.8% vs 57.0%), except for thrombocytopenia (12.9 % vs 0.2%), increased serum aminotransferase levels, and anemia. Adverse events leading to treatment discontinuation were higher for CAP plus LAP (10.7%) patients relative to T-DM1 (5.9%) patients. The rates of cardiac dysfunction adverse events were low and similar in both arms.

The study researchers concluded that T-DM1 should offer an important therapeutic option in the treatment of HER2-positive metastatic breast cancer patients. Final OS analysis (descriptive only) is expected in 2014.

Phase 3 Study of Crizotinib Versus Pemetrexed or Docetaxel Chemotherapy in Patients with Advanced ALK-Positive NSCLC

Written by ***Toni Rizzo***

Although single-agent second-line chemotherapy has limited efficacy in unselected non-small cell lung cancer (NSCLC), its effect in advanced anaplastic Kinase positive (ALK+) NSCLC is uncertain. Crizotinib has marked clinical activity in ALK+ NSCLC [Camidge DR et al. *Lancet Oncol* 2012; Kim DW et al. ASCO 2012. Abstract 7533]. The PROFILE 1007 [NCT00932893] trial, presented by Alice Tsang Shaw, MD, PhD, Dana-Farber Cancer Institute, Boston, Massachusetts, USA, compared the efficacy and safety of crizotinib with standard chemotherapy as second-line therapy in patients with advanced ALK+ NSCLC.

A total of 347 patients with previously treated stage IIIB/IV ALK+ NSCLC were randomized to crizotinib (250 mg BID, orally, 21-day cycle; n=173) versus pemetrexed