MedicalXpress

Researchers to present event-free and overall survival results from NeoALTTO trial

December 11 2013

Results from the initial analysis of event-free and overall survival for patients enrolled in the randomized, phase III Neoadjuvant Lapatinib and/or Trastuzumab Treatment Optimization (NeoALTTO) trial are to be presented here at the 2013 San Antonio Breast Cancer Symposium, held Dec. 10–14.

"NeoALTTO is a randomized, phase III clinical trial evaluating whether a combination of two HER2-targeted therapies, trastuzumab and lapatinib, given with standard paclitaxel chemotherapy before surgery [neoadjuvant therapy] is better than just one of the HER2-targeted therapies given with the same chemotherapy," said Martine Piccart-Gebhart, M.D., Ph.D., chair of the Breast International Group (BIG) in Brussels, Belgium. "We previously reported that the combination therapy resulted in more patients having a pathologic complete response.

"In San Antonio, we will present our analysis of whether improved pathologic complete response rates translate into better long-term outcomes for patients," continued Piccart-Gebhart. "I believe that our results will be vital for the process of drug development in the field of early HER2-positive breast cancer."

Neoadjuvant therapy is treatment given to shrink or eliminate a tumor before surgery. In some patients with breast cancer, neoadjuvant therapy effectively eliminates the tumor, and no invasive cancer is detectable in breast tissue and lymph nodes removed during surgery. These patients are said to have had a pathologic complete response.

In 2014, the results of NeoALTTO's "sister" trial, Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization (ALTTO), which is testing the effectiveness of dual treatment with trastuzumab and lapatinib after breast cancer surgery, will also become available, according to Piccart-Gebhart. "If the results of both studies are in line with each other, and depending on the strength of the results, we could witness a new standard of care for managing primary HER2-positive breast cancer," she said.

From January 2008 to May 2010, Piccart-Gebhart and colleagues enrolled in the NeoALTTO study 455 patients with HER2-positive primary breast cancer with tumors greater than 2 cm in diameter. Of those patients, 154 were randomly assigned to lapatinib, 149 to trastuzumab, and 152 to the combination. These HER2-targeted therapies were given alone for six weeks and then the chemotherapy paclitaxel was also administered for a further 12 weeks, at which point surgery was conducted. After surgery, patients received adjuvant chemotherapy followed by the same HER2-targeted therapy as in the neoadjuvant phase to complete 52 weeks. Follow-up is planned for 10 years after the last patient was randomized.

The researchers have previously reported that 51.3 percent of patients randomly assigned to neoadjuvant trastuzumab plus lapatinib had a pathologic complete response compared with 29.5 percent and 24.7 percent of patients randomly assigned to neoadjuvant trastuzumab and neoadjuvant lapatinib, respectively.

More information: Publication Number: S1-01

Presenter: Martine Piccart-Gebhart, M.D., Ph.D.

Title: The association between event-free survival and pathological complete response to neoadjuvant lapatinib, trastuzumab or their combination in HER2-positive breast cancer. Survival follow-up analysis

of the NeoALTTO study (BIG 1-06)

Background: The NeoALTTO study demonstrated a significantly higher breast pathological complete response (pCR) rate (NSABP definition – ypT0/is) with dual HER2 blockade using lapatinib and trastuzumab compared with single HER2 blockade using either lapatinib or trastuzumab (51.3% vs. 24.7% vs. 29.5%, respectively; pMaterial and Methods: From January, 2008, to December, 2009, 455 patients were randomized from 99 participating sites in 23 countries. Patients were randomized to receive either lapatinib 1500 mg/d (154 pts), or trastuzumab 4 mg/kg IV loading dose followed by 2 mg/kg IV weekly (149 pts), or lapatinib 1000 mg/d with trastuzumab for a total of 6 weeks (152 pts). After this biological window, patients continued on the same targeted therapy plus weekly paclitaxel 80 mg/m^2 for a further 12 weeks, until definitive surgery (total neoadjuvant therapy duration of 18 weeks). After surgery, patients received 3 cycles of adjuvant FEC followed by the same targeted therapy as in the biological window of the neoadjuvant phase for a further 34 weeks (to complete 52 weeks of anti-HER2 therapy), with on-going follow-up planned until 10 years after last randomised patient. Secondary objectives included disease-free survival and overall survival (OS). Following current practice and draft FDA recommendations for neoadjuvant trial endpoints, an amendment was made to the protocol secondary objectives (released in May 2013). DFS (from surgery) was replaced by event-free survival (EFS) from randomisation; OS from surgery was correspondingly replaced with OS from randomisation, and examination of the association between these survival endpoints and locoregional pCR (ypT0/is ypN0) was added as a secondary objective. EFS was defined as the time from randomization to first EFS event (breast cancer relapse, second primary malignancy or death without recurrence). OS was defined as the time from randomization to death from any cause.
Results: The clinical cut-off date for the first planned analysis of these secondary objectives was on 26 May 2013, three years after the date of

last surgery. Data cleaning is ongoing and analysis will be completed by November 2013. Results for EFS, OS and their association with pCR will be presented at the meeting.

Funding: GlaxoSmithKline is the sponsor of this trial.