

[1] Phase III randomized trial comparing doxorubicin and cyclophosphamide followed by docetaxel (AC T) with doxorubicin and cyclophosphamide followed by docetaxel and trastuzumab (AC TH) with docetaxel, carboplatin and trastuzumab (TCH) in HER2 positive early breast cancer patients: BCIRG 006 study.

Slamon D, Eiermann W, Robert N, Pienkowski T, Martin M, Pawlicki M, Chan M, Smylie M, Liu M, Falkson C, Pinter T, Fornander T, Shifan T, Valero V, Mackey J, Tabah-Fisch I, Buyse M, Lindsay MA, Riva A, Bee V, Pegram M, Press M, Crown J, on behalf of the BCIRG 006 Investigators. UCLA, Los Angeles, CA; GBG, Munchen, Germany; US Oncology, Dallas, TX; Maria Sklodowska-Curie (MSC) Centre, Warsaw, Poland; GEICAM, Madrid, Spain; MSC Institute, Krakow, Poland; Mount Hospital, Perth, Australia; Cross Cancer Institute, Edmonton, Canada; Sun Yat-Sen Cancer Center, Taipei, Taiwan; University of Alabama, Birmingham, AL; Petz Aladar County, Gyor, Hungary; OnkologyKliniken, Stockholm, Sweden; Sharp Healthcare, San Diego, CA; MD Anderson Cancer Center, Houston, TX; Sanofi-Aventis, Paris, France; IDDI, Brussels, Belgium; CIRG, Paris, France; USC, Los Angeles, CA; ICORG, Dublin, Ireland

Background: This study evaluates the benefit of two trastuzumab-based (H) regimens in HER2 amplified breast cancer with the intent of integrating H to maximize efficacy and minimize known cardiotoxicity.

Material and Methods: HER2 amplified (centralized FISH) patients with axillary lymph node (LN) positive or high risk LN negative were randomized to either AC (60/600 mg/m² q3wk x4) followed by T (100 mg/m² q3wk x 4) or two H-containing regimens; AC followed by T with H x 1 year (q1wk during chemo/q3wk during FUP) or TCarbo (75 mg/m² / AUC6 q3wk x 6) with H x 1 year. Patients were prospectively stratified by positive LN (0, 1-3 vs 4+) and hormone receptor (HR) status. Patients with HR+ tumors received hormonal therapy for 5 yrs after chemotherapy. The primary endpoint was disease-free survival (DFS) with 80% power (0.05 significance level) to detect an absolute difference of 7%. Secondary endpoints included OS, safety, including cardiotoxicity (symptomatic events -CHF, gr3/4 ischemia/infarction, gr3/4 arrhythmia- and asymptomatic LVEF decline). We report the results of the first planned, protocol-mandated interim analysis conducted after 322 events (breast cancer relapse, second primary malignancy or death).

Results: A total of 3222 pts (1073 in AC-T, 1074 in AC-TH and 1075 in TCH) were recruited between Apr 2001 and Mar 2004. At a median follow-up of 23 months, the two H-containing arms have both met the DFS endpt: hazard ratio of 0.49 with AC-TH, p-value=0.0000048 and 0.61 with TCH, p-value=0.00015 (as compared to AC-T). At this time, there is no statistically significant difference btw the two H-containing arms perhaps due to the small number of events currently separating them. Symptomatic cardiac events: AC-T: 1.2% vs AC-TH: 2.3%, p-value=0.046; AC-T vs TCH: 1.2%, p value=1.00. Absolute LVEF decline >15% and below lower limit of normal occurred in 0.6% pts in AC-T, 2.4% in AC-TH and 0.4% in TCH arms respectively (AC-T vs AC-TH (p=0.001); AC-T vs TCH (p=0.54)).

Discussion: Result of this trial confirms the benefit of H when combined with docetaxel (AC-TH) or with docetaxel and carboplatin (TCH) without an anthracycline. There are fewer severe cardiac adverse events when H is administered without prior A. Longer follow-up is needed in order to confirm whether non-A-based adjuvant H regimens will have efficacy comparable to A-based regimens.

Thursday, December 8, 2005 9:45 AM
General Session 1 (9:45 AM-10:45 AM)