Title: Ten year follow-up of the BCIRG-006 trial comparing doxorubicin plus cyclophosphamide followed by docetaxel (AC®T) with doxorubicin plus cyclophosphamide followed by docetaxel, and trastuzumab (AC®TH) with docetaxel, carboplatin and trastuzumab (TCH) in HER2+ early breast cancer patients

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Body: Background: The intent of the BCIRG-006 study was to assess the relative benefit and safety of two trastuzumab-based regimens compared to a then standard (non-trastuzumab) regimen in the adjuvant treatment of early HER2+ breast cancer. We present the final evaluation of the long-term results from this trial that was designed to determine how to maximize both efficacy and safety.

Material and Methods: Between April, 2001 and March, 2004, we randomized 3222 HER2+ breast cancer patients with axillary lymph node-positive or high risk node-negative disease, to either standard AC (60/600 mg/m2 q3wk x4) followed by T (100 mg/m2 q3wk x 4) (AC-T) or two trastuzumab-containing regimens. The trastuzumab-based regimens were AC followed by T with trastuzumab (H) x 1 year (AC-TH), or TCarbo (75 mg/m2 / AUC6 q3wk x 6) with H x 1 year (TCH). Patients were prospectively stratified by number of positive nodes (0, 1-3 vs 4+) and hormone receptor status. Patients with ER and/or PR positive (HR+) disease received hormone-directed therapy for 5 yrs post chemotherapy. The primary endpoint was disease-free survival (DFS). Secondary endpoints included overall survival (OS) and safety, with extensive cardiac evaluation (symptomatic events and asymptomatic LVEF declines).

Results: Baseline characteristics of all arms of the study population were well balanced. Of the 3222 patients (1073 in AC-T, 1074 in AC-TH and 1075 in TCH) initially randomized, we have efficacy and safety data with a median follow-up of 10.3 years. Of the original 3222 patients, 511 deaths occurred prior to study end while 1817 patients reached the 10 years follow-up point. During the study period, a total of 508 patients were lost to follow-up, 162 withdrew consent prior to 10 years and an additional 224 patients had missing data prior to 10 years. We will present the DFS benefit of the trastuzumab containing arms (AC-TH and TCH) compared to AC-T on this study population. We will also present cumulative data on the incidence of protocol-defined, symptomatic or significant asymptomatic cardiac events in each of the study arms and compare them to the 3- and 5-year study follow-up results.

Discussion: The BCIRG-006 10-year follow-up final results will contain an assessment of the relative long-term benefit and safety of adding trastuzumab to the adjuvant treatment of HER2+ early breast cancer, as well as the efficacy/safety of anthracycline versus non-anthracycline based regimens when combined with adjuvant trastuzumab.