for the L+C arm versus the C arm. Group differences in adjusted mean change from baseline, although not statistically significant ($p > 0.05$), were consistently in favor of the L+C arm and ranged from 0.7 to 2.2 (FACT-B), 0.9 to 1.5 (FACT-G), 0.2 to 1.5 (TOI), 0.00 to 0.03 (EQ-5 utility) and 0.3 to 1.8 (ED-5D VAS) over a 24-week follow up.

Conclusions: The two treatment groups appear to be similar in HRQOL scores, suggesting that there was no detriment to quality of life in patients receiving combination therapy (lapatinib plus capecitabine) compared with those receiving monotherapy (capecitabine) in this heavily pre-treated patient population.

566 Poster Discussion

Phase II evaluation of the efficacy and safety of trastuzumab plus pertuzumab therapy in patients with HER2-positive metastatic breast cancer that had progressed during trastuzumab treatment

J. Cortés[1], K. Gelmon[2], P. Fumoleau[3], A. Wardley[4], S. Verma[5], P.F. Conte[6], L. Gianni[7], S.J. Kirk[8], V. McNally[8], J. Baselga[1]. [1]*Vall d'Hebron University Hospital, Department of Oncology, Barcelona, Spain;* [2]*British Columbia Cancer Agency, Vancouver, Canada;* [3]*Centre Georges-François-Leclerc, Dijon, France;* [4]*Christie Hospital, Manchester, United Kingdom;* [5]*Ottawa Regional Cancer Center, Ottawa, Canada;* [6]*Divisione di Oncologia Medica, Modena, Italy;* [7]*Oncologia Medica, Milan, Italy;* [8]*Roche Products Limited, Welwyn, United Kingdom*

Background: Pertuzumab (P) is the first of a new class of HER dimerization inhibitors (HDI), targeting multiple HER pathways by binding to HER2 to block both homo- and heterodimerization of HER2 and other HER receptors. Trastuzumab (Herceptin®, H) binds to a different epitope and xenograft studies indicate that the complementary mechanisms of action of P and H have a synergistic effect when combined. This study investigates the efficacy and safety profile of H plus P in previously treated patients (pts) with HER2-positive MBC.

Material and Methods: Pts with measurable, centrally tested HER2-positive MBC who had received ⩽3 prior lines of therapy (including adjuvant therapy), had progressed during prior H treatment, and had a baseline LVEF ⩾55% that had not declined to <50% with H therapy, were eligible for this single-arm, Simon-type, two-stage trial. Consenting pts received H at 2 mg/kg qw (4 mg/kg loading dose [LD]) or 6 mg/kg q3w (8 mg/kg LD) plus P at 420 mg q3w (840 mg LD) starting within 9 weeks of the last dose of H. LVEF was regularly assessed.

Results: Currently 61 pts have received ⩾1 dose of therapy. Interim efficacy analysis in 33 eligible pts (⩾1 tumor evaluation on treatment) was: CR 1 (3%); PR 5 (15%); SD ⩾6 months 7 (21%); SD <6 months 10 (30%); and PD 10 (30%). Overall response rate was 18% and clinical benefit rate was 39%. Of 61 pts evaluable for safety, 54 had ⩾1 AE. Frequent (⩾30%) grade 1/2 AEs included diarrhea (59%), pain (43%), nausea/vomiting (36%), mucositis (33%), skin (31%), and rash (30%). Grade ⩾3 AEs included DVT, UTI, and rash (all n = 1) and in 1 pt, increased ALP, hyperbilirubinemia and hepatic failure. There was only one treatment-related grade 3 AE (diarrhea), which resolved and treatment was continued. Two pts experienced a fall in LVEF of ⩾10% to <50% (1 centrally confirmed). Both pts remained asymptomatic and were withdrawn from the study due to PD. No pts withdrew due to cardiac events or treatment-related AEs.

Conclusions: The combination of H plus P is active and well tolerated in pts with HER2-positive MBC that has progressed during prior H therapy. Most AEs were grade 1 or 2 and no clinically significant cardiac events were observed in 61 pts. Further studies are currently underway to fully evaluate the use of this agent in breast cancer.

567 Poster Discussion

Final results of a phase II study of bevacizumab plus docetaxel for the first-line treatment of metastatic breast cancer (TORI-B01)

S. Hurvitz[1], H.J. Allen[2], R.L. Moroose[2], D. Chan[2], C. Hagenstad[2], S.H. Applebaum[1], G. Patel[2], E.H. Hu[2], D.J. Slamon[1], F. Kabbinavar[1]. [1]*UCLA School of Medicine, Internal Medicine/Div of Heme-Onc, Los Angeles, USA;* [2]*Translational Oncology Research International, Oncology, Los Angeles, USA*

Background: First line treatment (Tx) of metastatic breast cancer (MBC) with paclitaxel (P) plus bevacizumab (B) significantly improves response rates (RR) and progression free survival (PFS) compared to P-alone. Docetaxel (D) is one of the most active agents for MBC, with RR between 30−60%. To assess the activity of D + B, a multicenter, phase II trial was begun. The primary endpoint was time to progression (TTP). Secondary endpoints were RR, duration of response, overall survival (OS) and safety.

Methods: Pts with Her2/neu negative MBC, previously untreated in the metastatic setting were eligible. Adjuvant Tx with a taxane was allowed if ⩾12 mos had lapsed since its completion. This trial began as a 2-arm study with a D-alone arm. When B became widely available, it was converted to a 1-arm, open-label trial of D+B and pts enrolled in the D-alone arm were given the option to cross-over to D+B. All pts received B 15 mg/kg IV and D 75 mg/m^2 IV q3 wks. Tx continued until disease progression (PD), unacceptable toxicity or consent withdrawal.

Results: From 3/2005 to 9/2006, 76 pts were enrolled. Two pts were ineligible. Seven pts were initially randomized to D-alone. Six of these pts chose to cross-over to D+B and are only included in the safety analysis. Efficacy data are based on the intent to treat (ITT) population of 67 pts. The median (med) pt age was 57. The confirmed objective RR is 50.7% (34/67) with 7.5% (5/67) complete responses (CR) and 43.3% (29/67) partial responses (PR). 19.4% (13/67) pts had stable disease (SD) as their confirmed best response. With 18.1 mos med follow up, the med TTP is 9.3 months, [95% CI (8.2, 12.4)]. The TTP for hormone receptor (HR)-negative tumors was 6.4 mos [95% CI (4.1, 8.2)] versus 12.6 mos [95% CI (9.3−15.8)] for HR(+) tumors (Log rank test $p = 0.0010$). The median OS is 25.7 mos [95% CI (20.1, NR)]. Six pts remain on study, including 1 pt who has completed 40 cycles thus far (range 20−40 cycles). The most common Gr 3/4 AEs were neutropenia (25/75), leukopenia (16/75), fatigue (14/75), hypertension (6/75), and infection (7/75). There were 2 cases of Gr 3/4 epistaxis, 1 Gr 3 proteinuria and 1 Gr 3 DVT.

Discussion: D + B was generally well-tolerated with no new safety concerns, manageable toxicity and promising efficacy results.

This study was supported by unrestricted research grants from Sanofi-Aventis & Genentech.

568 Poster Discussion

Phase III study of gemcitabine (G) plus paclitaxel (T) versus T in patients with metastatic breast cancer (MBC) – Post-study chemotherapy (PSC) trend analysis

A. Llombart[1], S. Nag[2], G. Calderillo-Ruiz[3], J. Rolski[4], A. Pluzanska[5], L. Simms[6], K. Look[6], J. Gill[6], A. Melemed[6], J. O'Shaughnessy[7]. [1]*Instituto Valenciano de Oncologia, Oncology, Valencia, Spain;* [2]*Jehangir Hospital, Oncology, Pune, India;* [3]*Instituto Nacional de Cancerologia, Oncology, Mexico City, Mexico;* [4]*Oncological Institute, Oncology, Krakow, Poland;* [5]*Klinika Chemioterapii, Oncology, Lodz, Poland;* [6]*Eli Lilly and Company, Lilly Oncology, Indianapolis, USA;* [7]*Baylor-Sammons Cancer Center, Oncology, Dallas, USA*

Background: This Phase III trial was designed to compare safety and efficacy of G plus T versus single-agent T in patients (pts) with MBC. Earlier reports of this trial described a statistically significant advantage in response, time-to-progression and overall survival (OS) for the GT combination with a manageable toxicity profile. While the benefits of first-line chemotherapy for MBC are well established, the clinical impact of second and multi-line chemotherapy remains controversial. We performed an exploratory analysis of PSC and the effect of PSC on OS for pts in the current Phase III trial.

Materials and Methods: Pts enrolled with unresectable MBC, one prior regimen of anthracycline-based chemotherapy, and KPS ⩾70 were randomized to receive either GT (G 1250 mg/m^2 D1, 8; T 175 mg/m^2 D1) or T (175 mg/m^2 D1) every 21 days until disease progression (PD) or undue toxicity. After completing treatment, pts with PD were given follow-up assessments every 4 months until a total of 440 death events were recorded (the analysis reported here). Details of any PSC were recorded at each visit. Survival results were analyzed by the Kaplan–Meier and Cox proportional hazards methods.

Results: Following study discontinuation, 56% of pts in the GT arm and 60% of pts in the T arm received at least one line of PSC and 20% of pts in both arms received ⩾3 lines. Use of single-agent PSC was more common in both treatment arms (GT, 69%; T, 62%) compared with combination PSC. Pts received over 25 different PSC agents. The most common PSC agents were vinorelbine (GT, 32%; T, 35%), capecitabine (GT, 28%; T, 22%), docetaxel (GT, 15%; T, 14%), 5-fluorouracil (GT, 11%; T, 17%), and gemcitabine (GT, 5%; T, 17%). For pts receiving PSC, median OS was 20.2 months in the GT arm and 18.9 months in the T arm. For pts not receiving PSC, median OS was 14.2 months in the GT arm and 10.5 months in the T arm. Comparison of PSC versus no PSC in the GT arm produced a hazard ratio (HR) of 0.84 (95% CI: 0.64−1.10; $p = 0.197$). However, comparison of PSC versus no PSC in the T arm had a HR of 0.66 (95% CI: 0.5−0.86; $p = 0.003$).

Conclusions: Over 40% of pts receiving first-line GT or T did not receive PSC. Exploratory analysis of OS did not find significant evidence that OS for GT-treated pts was impacted by PSC. However, T-treated pts not receiving PSC had a significantly reduced survival outcome. The implications of these results will be discussed.