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P5-19-03 Albumin-Bound Paclitaxel (ab-pac) Versus Docetaxel for First-Line Treatment of Metastatic Breast Cancer (MBC): Overall Survival and Safety Analysis of a Randomized Phase II Trial

WJ Gradishar, D Krasnojon, S Cheporov, AN Makhson, GM Manikhas, A Clawson, P Bhar

Gradishar and colleagues provided updated results of an open-label, multicenter, phase II study that evaluated the safety and efficacy of different dosing regimens of albumin-bound paclitaxel (*nab*-paclitaxel; Abraxane, Celgene) and docetaxel in the first-line metastatic breast cancer (MBC) treatment setting. Patients were randomized to 1 of the following: *nab*-paclitaxel 300 mg/m^2 every 3 weeks (q3w [arm A; n=76]), *nab*-paclitaxel 100 mg/m^2 the first 3 of 4 weeks (qw 3/4 [arm B; n=76]), *nab*-paclitaxel 150 mg/m^2 qw 3/4 (arm C; n=74), and docetaxel 100 mg/m^2 q3w (arm D; n=74). The longest median overall survival (OS) was 33.8 months in arm C (27.7 months, 22.2 months, and 26.6 months for arms A, B, and D, respectively). Progression-free survival (PFS) was 14.6 months in arm C, compared with 10.9 months, 7.5 months, and 7.8 months for arms A, B, and D, respectively. The safety profile of *nab*-paclitaxel was consistent with previous reports, with grade 3 neuropathy occurring most frequently in arm C (21%, 9%, 22%, and 12% for arms A, B, C, and D, respectively; *P*=.083). Among patients who received *nab*-paclitaxel 150 mg/m^2 (arm C), the best response occurred at cycle 2, whereas dose reductions due to toxicities occurred at later treatment cycles. Dose reductions occurred in 18%, 17%, 47%, and 28% of patients in arms A, B, C, and D, respectively. The researchers concluded that a 150-mg/m^2 weekly dose of *nab*-paclitaxel may help patients achieve a clinical response before the onset of dose-limiting adverse events.

S3-7 Everolimus for Postmenopausal Women With Advanced Breast Cancer: Updated Results of the BOLERO-2 Phase III Trial

GN Hortobagyi, M Piccart, H Rugo, H Burris, M Campone, S Noguchi, M Gnant, KI Pritchard, L Vittori, P Mukhopadhyay, T Sahmoud, D Lebwohl, J Baselga

The pivotal phase III BOLERO-2 (Breast Cancer Trials of Oral Everolimus) trial enrolled 724 postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer who recurred or progressed while on or following previous treatment with letrozole or anastrozole. Patients received oral exemestane (Aromasin, Pfizer) 25 mg daily with either everolimus (Afinitor, Novartis) 10 mg daily (n=485) or placebo (n=239). The updated analysis by Hortobagyi and associates was based on a median follow-up of 12.5 months. Investigator-assessed PFS revealed a hazard ratio (HR) of 0.44 (95% confidence interval [CI], 0.36–0.53) and a median duration of 7.4 months (everolimus + exemestane) versus 3.2 months (exemestane alone). Twelve-month estimates of patients without disease progression were 31% and 10% in the everolimus plus exemestane and exemestane-alone arms, respectively. An additional analysis based on an independent central radiology review showed that everolimus extended PFS to 11 months compared to 4.1 months, and 12-month estimates of patients without disease progression were 48% and 18%, respectively. Response rates and clinical benefit rates were higher for patients who received everolimus plus exemestane versus exemestane alone (12% vs 1.3% and 50.5% vs 25.5%, respectively). Side effects were consistent with those previously reported with everolimus. Everolimus increased exemestane steady-state Cmin and Cmax levels by 45% and 64%, respectively, with no difference in estradiol levels. Serum markers of bone resorption and bone formation increased in the exemestane-alone arm, and typically decreased in the everolimus plus exemestane arm.

S5-5 A Phase III, Randomized, Double-Blind, Placebo-Controlled Registration Trial To Evaluate the Efficacy and Safety of Pertuzumab + Trastuzumab + Docetaxel vs. Placebo + Trastuzumab + Docetaxel in Patients with Previously Untreated HER2-Positive Metastatic Breast Cancer (CLEOPATRA)

J Baselga, SB Kim, SA Im, R Hegg, YH Im, L Roman, JL Pedrini, J Cortés, A Knott, E Clark, GA Ross, SM Swain

In the randomized, double-blind, placebo-controlled phase III CLEOPATRA (Clinical Evaluation of Pertuzumab and Trastuzumab) study, Baselga and coworkers evaluated the efficacy and safety of pertuzumab combined with

trastuzumab (Herceptin, Genentech) and chemotherapy compared to trastuzumab and chemotherapy alone in 808 patients with centrally confirmed, HER2-positive, metastatic or locally recurrent, unresectable breast cancer. Patients received placebo plus trastuzumab and docetaxel (control group) or pertuzumab plus trastuzumab and docetaxel (pertuzumab group) until disease progression or unmanageable toxicities occurred. The median PFS was 12.4 months in the control group versus 18.5 months in the pertuzumab group (P<.001). The interim analysis of OS was performed after 165 events had occurred, and survival data were incomplete at the time of presentation. The overall response rate (ORR) was 80.2% in the pertuzumab group versus 69.3% in the control group (P=.0011). Grade 1/2 diarrhea, rash, mucosal inflammation, febrile neutropenia, and dry skin were more common in the pertuzumab group, and typically occurred during concomitant docetaxel administration. Grade 3 or higher febrile neutropenia and diarrhea were also increased in the pertuzumab group. Study results were simultaneously published in the December 9 online edition of the *New England Journal of Medicine*.

S1-1 A Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First-Line Therapy for Postmenopausal Women With Metastatic Breast Cancer: SWOG S0226

RS Mehta, WE Barlow, KS Albain, T Vandenberg, SR Dakhil, NR Tirumali, DL Lew, DF Hayes, JR Gralow, RB Livingston, GN Hortobagyi

In a randomized phase III trial by Mehta and associates, 707 postmenopausal MBC patients received anastrozole (Arimidex, AstraZeneca), either alone or in combination with fulvestrant (Faslodex, AstraZeneca). The median PFS was 13.5 months in the anastrozole-alone arm versus 15 months in the anastrozole plus fulvestrant arm (HR, 0.80; 95% CI, 0.68–0.94). Patients treated with anastrozole plus fulvestrant had a median OS of 47.7 months, compared with 41.3 months for patients treated with anastrozole alone (HR, 0.81; 95% CI, 0.65–1.00). Patients with no prior tamoxifen treatment (60%, n=414) had a median PFS of 12.6 months in the anastrozole-alone arm compared with 17 months in the anastrozole plus fulvestrant arm. Patients who received prior tamoxifen treatment had a median PFS of 14.1 months and 13.5 months for the anastrozole-alone arm and the anastrozole plus fulvestrant arm, respectively. Grade 3 toxicities were reported in 11.4% of patients in the anastrozole-alone arm and in 13.3% of patients in the anastrozole plus fulvestrant arm. Three deaths, 1 grade 4 pulmonary embolism, and 1 grade 4 neutropenia and lymphopenia also occurred in the anastrozole plus fulvestrant arm. Grade 4 toxicities occurred in 4 patients in the anastrozole-alone arm. Only 4 patients in the anastrozole monotherapy arm and 11 patients in the combination arm discontinued treatment due to toxicity.

P5-19-13 A Randomized Phase II Trial of First-Line Metastatic Breast Cancer (MBC) Patients: Sub-Set Analysis of Albumin-Bound Paclitaxel (ab-pac) Given Weekly at 150 mg/m^2

WJ Gradishar, D Krasnojon, S Cheporov, AN Makhson, GM Manikhas, A Clawson, P Bhar

An open-label, multicenter, randomized phase II trial evaluated the efficacy and safety of 3 different dosing regimens of *nab*-paclitaxel versus docetaxel for the first-line treatment of 300 MBC patients. Gradishar and colleagues reported updated results for the 74 patients who were treated with *nab*-paclitaxel at 150 mg/m^2 qw 3/4. Of that subset, 35 patients (47%) required a dose reduction due to toxicity. Investigator-assessed ORR and PFS were numerically higher in patients who had dose reductions (ORR, 80%; median PFS, 14.8 months) versus patients whose dosing remained the same (ORR, 69%; median PFS, 12.8 months). The median OS was 33.8 months for all patients in the subset, 35.2 months for patients who had dose reductions, and 31.8 months for patients without dose reductions. Patients in whom the dose was reduced received a median of 10 cycles of treatment compared with 8 cycles in patients without dose reductions.

S5-7 A Phase 2, Randomized, Open-Label, Study of Neratinib (HKI-272) vs Lapatinib Plus Capecitabine for 2nd/3rd-Line Treatment of HER2+ Locally Advanced or Metastatic Breast Cancer

M Martin, J Bonneterre, CE Geyer, Jr., Y Ito, J Ro, I Lang, S-B Kim, C Germa, J Vermette, ML Vo Van, K Wang, A Awada

Martin and colleagues presented results from a phase II, randomized, open-label study of neratinib (Puma Biotechnology, Inc.) versus lapatinib (Tykerb, GlaxoSmithKline) in combination with capecitabine (Xeloda, Genentech) in patients with HER2-positive, metastatic or locally advanced breast cancer. Patients had disease progression following prior treatment with trastuzumab and taxane chemotherapy. Patients received either neratinib 240 mg daily (n=117) or lapatinib 1,250 mg daily plus capecitabine 1,000 mg/m^2 twice daily on days 1–14 of each 21-day cycle (n=116). For patients in the neratinib arm versus the lapatinib plus capecitabine arm, respectively, 2% and 4% experienced a complete response, 27% and 36% experienced a partial response, and 15% and 23% had stable disease for more than 6 months. The ORR for the neratinib arm was 29%, compared with 40% for the lapatinib plus capecitabine arm. There was a clinical benefit rate of 44% and 63%, respectively. Median PFS was 4.5 months in the neratinib arm and 6.8 months in the lapatinib plus capecitabine arm (P=.231). No unexpected toxicities were reported.