

Highlights From the American Society of Clinical Oncology 2011 Breast Cancer Symposium

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275 Albumin-bound paclitaxel (ab-pac) versus docetaxel for first-line treatment of metastatic breast cancer (MBC): final overall survival (OS) analysis of a randomized phase II trial

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

Gradishar and colleagues provided updated results of a phase II study that evaluated 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 4 treatment arms: *nab*-paclitaxel 300 mg/m² every 3 weeks (arm A; n=76), *nab*-paclitaxel 100 mg/m² the first 3 of 4 weeks (arm B; n=76), *nab*-paclitaxel 150 mg/m² the first 3 of 4 weeks (arm C; n=74), and docetaxel 100 mg/m² every 3 weeks (arm D; n=74). Response rates were highest in the arm receiving *nab*-paclitaxel 150 mg/m² (arm C). The longest median overall survival (OS) was 33.8 months in arm C, compared with 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 overall response rate (ORR) was 74% in arm C, compared with 46%, 63%, and 39% 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*=.082). Grade 4 neutropenia and grade 3 fatigue were most prevalent in the docetaxel treatment arm.

289 A multicenter, open-label phase II trial of dovitinib, a fibroblast growth factor receptor 1 (FGFR1) inhibitor, in FGFR1-amplified and nonamplified metastatic breast cancer (BC)

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Andre and colleagues examined the novel targeted agent dovitinib (Novartis) in an open-label phase II trial among patients with human epidermal growth factor receptor 2 (HER2)-negative MBC. Based on fibroblast growth factor receptor 1

(FGFR1) status and hormone receptor (HR) tumor subtype, patients were stratified into the following groups: FGFR1+, HR+ (group 1); FGFR1+, HR- (group 2); FGFR1-, HR+ (group 3); and FGFR1-, HR- (group 4). Patients received 500 mg of oral dovitinib once per day in a 5-days-on, 2-days-off schedule. The primary endpoint was best ORR according to response evaluation criteria in solid tumors (RECIST) in patients with measurable disease per external radiology review. As of January 2011, data from 77 out of 81 treated patients were available. Liver metastases were present in 58% of patients (81%, 50%, 50% in groups 1, 3, 4, respectively). The median exposure time to dovitinib was 1.7 months (range, 0–8.2 months); 8 patients received more than 4 months of therapy. Of the patients with measurable disease at baseline, 13% of patients in group 1 had unconfirmed partial responses. Stable disease of 4 months or longer was observed in 44%, 29%, and 11% of patients in groups 1, 3, and 4, respectively. The most common adverse events (AEs) were vomiting (75%; 6% grade 3), diarrhea (72%; 6% grade 3), nausea (62%; 5% grade 3), and asthenia (61%; 17% grade 3). This is the first study to demonstrate the potential value of an FGFR1 inhibitor in patients with FGFR1-amplified breast cancer. Treatment with dovitinib produced antitumor activity in patients with HR+, FGFR1- amplified breast cancer, and other subgroups had disease stabilization. Future studies are planned to further evaluate dovitinib treatment in patients with HR+ breast cancer.

283 A phase II neoadjuvant trial of concurrent trastuzumab and paclitaxel without anthracycline in women with HER2-positive operable breast cancer

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Jinno and coworkers investigated whether the administration of trastuzumab (Herceptin, Genentech) and paclitaxel without anthracycline as neoadjuvant chemotherapy is efficacious in women with HER2-positive operable breast cancer. The researchers also analyzed predictive factors of partial complete response (pCR), such as deregulation of the phosphatidylinositol 3-kinase (PI3K) pathway. Prior to surgery, 37 patients with HER2-positive operable breast cancer received 12 cycles of weekly paclitaxel (80 mg/m² intravenously [IV]) plus weekly trastuzumab (4 mg/kg loading dose followed by 2 mg/kg IV). Estrogen

receptors (ER) and progesterone receptors (PgR) were positive in 18 and 16 patients, respectively. The ORR was 86.5%. Absence of residual invasive carcinoma in the breast was considered a pCR. The pCR rate was 48.6% and notably associated with PgR negativity ($P=.004$) and higher Ki-67 ($P=.01$). Among the 13 tumors examined, there was a *PIK3CA* mutation frequency of 30.8%, and phosphatase and tensin homolog (PTEN) loss occurred in 33%. No significant correlations were observed among pCR rate and PTEN loss and/or *PIK3CA* mutation. The investigators concluded that combination trastuzumab and paclitaxel without anthracycline achieves a high pCR rate and is effective as neoadjuvant chemotherapy in women with HER2-positive operable breast cancer.

268 Results of ENCORE 301, a randomized, phase II, double-blind, placebo-controlled study of exemestane with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptor-positive (ER+) breast cancer progressing on a nonsteroidal aromatase inhibitor (AI)

DA Yardley, R Ismail-Khan, P Klein

Suppression of the growth factor signaling pathways that mediate aromatase inhibitor (AI) resistance has been observed with the use of entinostat. Yardley and associates studied the addition of entinostat (Syndax Pharmaceuticals) to exemestane therapy in postmenopausal women with locally recurrent or ER-positive MBC who had progressed on a nonsteroidal AI for its impact on PFS. A total of 130 patients were enrolled, with the following inclusion criteria: all patients had received prior hormonal therapy (58% had received more than 1 prior therapy), 62% had received prior chemotherapy, all but 1 patient had Stage IV disease, and 82% had measurable disease. Patients were randomized to exemestane 25 mg daily plus entinostat 5 mg ($n=64$) or placebo ($n=66$) weekly. Treatment with entinostat significantly improved PFS (4.28 vs 2.27 months, respectively; hazard ratio [HR], 0.73; $P=.06$) and reduced the risk of disease progression by 27%. The rate of serious AEs was similar between groups (13% in the entinostat group vs 12% in the placebo group). Based on the positive study results thus far, a phase III trial is planned to further evaluate the addition of entinostat to exemestane therapy.

273 Gemcitabine (G) and cisplatin (C) as first-line treatment of metastatic breast cancer (MBC): results of phase II trial

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A phase II trial by Karthaus and colleagues sought to determine the objective tumor response rate of combination

gemcitabine and cisplatin as first-line treatment of MBC. A total of 70 female patients with MBC were enrolled. There were 67 patients, who received a total of 310 cycles (1 cycle=21 days, with treatment administered on days 1 and 8) of gemcitabine (1,000 mg/m²) and cisplatin (35 mg/m²); 54 of these patients were evaluable. Complete, partial, and overall responses were observed in 13%, 35.2%, and 48.2% of evaluable patients, respectively. Disease stabilization was observed in 35.2% of patients. Disease progression occurred in 9.3% of patients; time to progression was 33.9 weeks (95% confidence interval [CI], 23.9–48.0). The OS was 84 weeks (95% CI, 58.6–119.3), with a 1-year OS rate of 68.4% (95% CI, 53.6–79.3%). Grade 4 toxicities included neutropenia (14.9%; 10 of 67 patients) and hypotension (1.5%).

269 Final results of NKTR-102, a topoisomerase I inhibitor-polymer conjugate, in patients (Pts) with pretreated metastatic breast cancer (MBC) demonstrating significant antitumor activity

A Garcia, A Awada, S Chan, GHM Jerusalem, RE Coleman, MT Huizing, A Mehdi, SM O'Reilly, JT Hamm, PJ Barrett-Lee, V Cocquyt, K Sideras, DE Young, M Brown, C Zhao, AL Hannah, ACF Leung, LK Masuoka, EA Perez

Garcia and coworkers examined the topoisomerase I inhibitor-polymer conjugate NKTR-102 in a phase II trial that compared 2 dosing regimens among 70 patients with pretreated MBC. The median age of patients was 55 years. Patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 (40%) or 1 (60%). Prior adjuvant or neoadjuvant therapy (median of 2 prior cytotoxic regimens) was administered in 74% of patients with MBC. All patients had received prior taxane treatment, 89% had prior anthracycline treatment, and 26% had prior anthracycline/capecitabine treatment. Patients were randomized to receive NKTR-102 145 mg/m² given as a 90-minute infusion every 14 days or every 21 days. The median PFS was 3.5 months for the 14-day arm compared with 5.3 months for the 21-day arm, with a total PFS of 4.6 months. The OS for the 14-day arm was 8.8 months versus 13.1 months for the 21-day arm; the total OS was 10.3 months. The ORR was 29%. Toxicity was manageable, and most AEs were grade 1 or 2. Diarrhea was the most common grade 3 toxicity (20% in the 14-day arm vs 23% in the 21-day arm), typically emerging after 3 months of treatment. Discontinuation due to AEs occurred in 20% of patients in the 14-day arm and 14% of patients in the 21-day arm. No patients had neuropathy, and alopecia was minimal in both arms (20% vs 11%, respectively). Based on the significant anti-tumor activity demonstrated by NKTR-102 in this setting, there are plans for a phase III study involving MBC patients who have had prior treatment with taxanes.