There were 8 *HER2*/*ERBB2* mutations in 7 patients; 2 of the 8 *HER2* mutations were previously shown to be activating mutations [Bose R et al. *Cancer Discov*. 2013]. A patient in the THL arm with HER2-enriched with V777L, preclinically predicted sensitive to L, had pCR. A patient in the TL arm with luminal A with L755S, preclinically predicted resistant to L, did not have pCR.

TP53 was the most frequently mutated gene in this cohort and was associated with increased pCR and a higher somatic mutation rate. Activating *HER2* mutations were uncommon but behaved as predicted from preclinical studies. Future studies to use genomic signatures, somatic mutations, and clinical variables for pCR predictions are underway.

ICE: No Advantage to Adding Capecitabine to Ibandronate in High-Risk Early BC

Written by Lynne Lederman

Elderly individuals are underrepresented in clinical trials. Standard anthracycline or taxane-based adjuvant regimens for breast cancer (BC) are often considered to be intolerable in frail elderly patients, whereas capecitabine has an acceptable toxicity profile and relevant single-agent activity in metastatic BC [O'Shaughnessy JA et al. *Oncologist*. 2012]. Elderly patients have a high incidence of treatment-induced osteopenia/osteoporosis, fractures, and bone surgery, especially from aromatase inhibitors [Chen JS et al. *Osteoporos Int*. 2009]. Adjuvant bisphosphonates reduce distant recurrence and increase overall survival (OS) in postmenopausal patients [Coleman R et al. SABCS 2013 (abstr S4-07)]. Therefore, the effects of adjuvant ibandronate with and without capecitabine was investigated in elderly patients.

Results of the phase 3 Study in Elderly Patients With Early Breast Cancer [ICE; NCT00196859] were reported by Gunter von Minckwitz, MD, PhD, University of Frankfurt, Frankfurt, and Chairman of the German Breast Group (GBG), Germany. This study enrolled 1358 women aged ≥ 65 years with moderate- to high-risk early BC who did not have extensive comorbidities. Patients were randomly assigned to capecitabine 2000 mg/m^2 daily on day 1 to 14 every 3 weeks for 6 cycles plus oral ibandronate 50 mg daily or 6 mg IV every 4 weeks (route of administration chosen by patients) for 2 years, or to ibandronate monotherapy for 2 years. Anastrozole and/or tamoxifen treatment in hormone receptor–positive disease and/or radiotherapy was started after capecitabine. Trastuzumab was not given.

Table 1. Invasive Disease–Free and Overall Survival, Median Follow-Up 61.3 Months

	Capecitabine + Ibandronate	Ibandronate
Invasive disease–free at 3 y	85.4	84.3
Invasive disease–free at 5 y	78.8	75.0
Ibandronate to combination	HR, 1.04; 95% CI, 0.84 to 1.29; *P* = .7012	
Overall survival at 3 y	95.4	94.3
Overall survival at 5 y	90.1	87.6
Ibandronate to combination	HR, 1.14; 95% CI, 0.85 to 1.54; *P* = .3827	

Data in percentage unless otherwise indicated.

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The primary end point was invasive disease–free survival (IDFS). Secondary end points were OS, bone-related events (fractures, surgery, or new osteoporosis; bone metastases were excluded), preference of oral or IV administration of ibandronate, and safety.

Patient and tumor characteristics were well balanced between the combination (n = 677) and monotherapy (n = 681) intent-to-treat arms. Median age was 71 years, with about 25% aged ≥ 75 years. About half of patients had node-positive disease; 81% were hormone-receptor positive, and almost three-quarters received aromatase inhibitors only; 75.8% in each arm completed ibandronate treatment, and 83.3% completed 6 cycles of capecitabine with 7.8% discontinuations due to toxicity. Of the 65.4% who started oral ibandronate, 2.4% switched from oral to IV; of the 34.6% who started with IV, 3.6% switched to oral; and the median duration of ibandronate was similar in the 2 treatment arms.

Toxicities in the capecitabine arm were as expected, including 31.0% of patients experiencing any grade 3 or 4 adverse events; fewer experienced skin disorders, especially hand-foot syndrome (14.6%). Bone-related events occurred in 25.0% of the capecitabine arm and 24.7% of the ibandronate-only arm (*P* = .65).

IDFS and OS are shown in Table 1. Neither treatment was favored in a subgroup analysis. Prof von Minckwitz suggested that given the high OS rate, patient life expectancy in this elderly population should be taken into account when treatment decisions are made.

The ICE study failed to show that adjuvant capecitabine improved IDFS in patients receiving ibandronate. The outcome of elderly patients with moderate- or high-risk early BC receiving ibandronate alone is favorable, although bone-related events were frequent (25%). Longer follow-up may be needed to observe any potential late effects of capecitabine.