

Among the key presentations:

- How to manage residual breast cancer: give more chemo
- Breast-conserving therapy trumps mastectomy at 10 years
- Adjuvant denosumab boosts disease-free survival, not just bone health
- Narrow is okay if breast cancer margin is negative
- Aromatase inhibitor or tamoxifen for DCIS — may depend on the patient
- Carboplatin for early triple-negative disease? One yes, one no
- Heart failure meds may protect the heart during trastuzumab treatment

A 'Major, Major Finding' in Managing Residual Breast Cancer

What should clinicians do when a patient with HER2-negative breast cancer has residual disease at surgery after neoadjuvant chemotherapy? Give even more chemotherapy, hints a study from Japan. The study showed that adding capecitabine (Xeloda, Roche) to adjuvant therapy such as tamoxifen extended disease-free and overall survival for women with HER2-negative breast cancer that was not fully eradicated by neoadjuvant chemotherapy and surgery. "The balance of benefit and toxicity would favor the use of capecitabine in the postneoadjuvant chemotherapy situation, but prediction for the therapeutic benefit needs to be investigated further," reported Masakazu Toi, MD, PhD, from Kyoto University Hospital in Japan. "I was very impressed and surprised with the outcomes because I don't think the majority of us thought that giving more chemotherapy would be beneficial," noted Virginia Kaklamani, MD, from the University of Texas Health Science Center San Antonio, who is a meeting codirector. She called the results "a major, major finding."

Ten-Year Data: Lumpectomy and Radiotherapy Trump Mastectomy

Lumpectomy with radiotherapy might be a better option than mastectomy, according to 10-year data from a retrospective study of more than 37,000 women in the Netherlands. The relative risk for death after 10 years was nearly 20% lower in women who underwent breast-conserving therapy (BCT) than in those who had mastectomy alone. The 10-year rate of overall survival was better with BCT than with mastectomy (76.8% vs 59.7%). In the BCT group, overall survival benefits extended across tumor size (T1 and T2) and nodal status (N0 and N1). This study is important, in part, because it provides 10-year data, noted study author Sabine Siesling, PhD, senior researcher at the Netherlands Comprehensive Cancer Organization in Utrecht. Most recent observational studies, which have also shown better survival with BCT, have been limited to 5 years of post-treatment data, which is "quite short" for breast cancer, she noted. "The main take-away message is that breast-conserving therapy should be the treatment of choice, especially in small tumors, when it is medically feasible," Dr Siesling concluded.

Denosumab Boosts Survival, Not Just Bones, in Breast Cancer

Adjuvant denosumab, a monoclonal antibody, appears to have life-preserving, not just bone-preserving, benefits in postmenopausal women with nonmetastatic breast cancer, according to the phase 3 placebo-controlled ABSCG-18 trial. "It's the first time ever that the antibody demonstrated disease-free-survival benefit," said lead investigator Michael Gnant, MD, from the Medical University of Vienna. In an intention-to-treat analysis, the impact of denosumab on disease-free survival reached borderline significance (hazard ratio, 0.82), "but a sensitivity analysis showed that that may be a conservative estimate," Dr Gnant reported. "In absolute numbers, the benefit is about 1% after 3 years, 2% after 5 years, and 3% at 7 years of follow-up," he said. Exploratory subgroup analyses hint that the benefit increases when denosumab is employed early, along with aromatase inhibitor therapy, and that the benefit is greater in patients with larger tumors and ductal histology.

Narrow Is Okay If Breast Cancer Margin Is Negative

Any negative surgical margin, no matter how narrow, is a good thing for patients with invasive breast cancer who undergo breast-conserving surgery, results from a massive study show. The incidence of ipsilateral breast tumor recurrence (IBTR) was similar in 11,900 Danish women who underwent initial breast-conserving surgery or re-excision, whether they had wide negative margins (2 to 4 mm) or narrow negative margins (0 to <1 mm). The risk for IBTR in the overall cohort was 2.4% at 5 years and 5.9% at 9 years. There were no significant differences in IBTR among any patient with negative margins, no matter how close a shave their tumors had. However, a final positive margin of any width was associated with a 2.5-fold risk for IBTR, reported Anne Bodilsen, a PhD candidate at Aarhus University Hospital in Denmark. "The increased risk for [IBTR with] re-excision was just for the patients who had residual tumor left," she said. Notably, negative-margin width did not translate into differences in overall survival.

AI vs Tamoxifen for DCIS? A Toss-up, Unless...

Oncologists can offer postmenopausal women with ductal carcinoma in situ (DCIS) two options to prevent breast cancer recurrence: anastrozole (Arimidex, AstraZeneca), which might suit some younger women; or tamoxifen (multiple brands), which might be the drug of choice for some older women. Either drug would be a good selection for the majority of patients, suggest results from two randomized placebo-controlled trials involving nearly 4200 patients. Both the IBIS-II DCIS trial and the NRG/Oncology/NSABP B-35 trial show that anastrozole and tamoxifen are comparably efficacious for preventing recurrence of both DCIS and invasive breast cancers in postmenopausal women. However, each drug has a distinct adverse-event profile, which could drive drug choice in individual patients. Overall, there's no clear differences in efficacy — a slight favor, I think, in terms of anastrozole when you look at all of the data," said Jack Cuzick, PhD, from Queen Mary University of London, United Kingdom, and lead author of the IBIS-II DCIS trial.

Cardiac Meds Appear to Protect Heart Against Herceptin Damage

Breast cancer patients treated with trastuzumab (Herceptin, Roche) have a lower risk for left ventricular (LV) dysfunction and consequent treatment interruptions when treated prophylactically with standard heart failure medication, according to a study that was terminated early because of positive results and could have practice-changing implications, noted lead investigator Edith Pituskin, RN, PhD, from the University of Alberta in Calgary, Canada. Trastuzumab-related cardiac toxicity "is frequent and potentially lethal" in breast cancer

patients, she noted, and there are no effective prevention strategies to date. In the MANICORE study, multivariate analysis indicated that use of both the beta blocker bisoprolol and the angiotensin-converting-enzyme inhibitor perindopril significantly predicted preserved LV function, the study's secondary outcome. Paradoxically, neither drug prevented change from baseline in LV end-diastolic volume, also known as LV remodeling, which was the study's primary outcome. Nevertheless, the use of the heart drugs "may provide additional safety," said Dr Pituskin.

Carboplatin for Early TNBC? Depends on Who You Ask

The addition of carboplatin to a standard neoadjuvant chemotherapy regimen significantly improves disease-free and event-free survival in patients with early-stage triple-negative breast cancer (TNBC), according to one study presented here by Gunter von Minckwitz, MD, from Heidelberg University Hospital in Germany. But another study, conducted in the United States, suggests that it doesn't. Well-designed trials in the neoadjuvant setting will be required before carboplatin can be recommended as routine therapy in early TNBC, said invited discussant Angela M. DeMichele, MD, from the University of Pennsylvania School of Medicine in Philadelphia. "I would say it's still an individualized decision. The hazard ratios suggest benefit, but currently there are not enough data to be conclusive. Moreover, the chemotherapy backbone and carboplatin dosing schedules may be critical to optimal efficacy, and we still don't know the long-term effect of the added toxicities of this drug," Dr DeMichele explained. These studies "don't seem to support going home and routinely adding platinum to the neoadjuvant chemotherapy regimens, and the decision to use it should be individualized for an appropriate given patient," said Steven J. Isakoff, MD, PhD, from the Massachusetts General Hospital Cancer Center in Boston.

Skip Chemo in Young Women With Common Breast Cancer Subtype?

Older women with the luminal A subtype of breast cancer can consider skipping chemotherapy altogether and still expect a good prognosis, even when they are node positive, according to a new analysis of an old Danish study. "This is clearly part of a body of evidence [in breast cancer] that's building up.... We can probably back off on the aggressiveness of our treatments and still achieve the same results," said investigator Torsten Nielsen, MD, PhD, from the University of British Columbia in Vancouver, Canada. The findings raised some eyebrows, given that chemotherapy is considered standard in premenopausal breast cancer. But the question is a relevant one, noted Virginia Kaklamani, MD, from the University of Texas Health Science Center San Antonio. Dr Kaklamani, an investigator in an ongoing prospective study that is examining a similar question, said that the Danish Breast Cancer Cooperative Group 77B study results "confirm what we thought — that we kind of don't need chemotherapy for these patients."

Neratinib Keeps Benefiting Herceptin-Treated Breast Cancer

New results from the ExteNET study of the investigational drug neratinib after adjuvant trastuzumab confirm a benefit of the agent beyond the previously reported 2-year results, researchers reported here. "The 3-year exploratory analysis is consistent with previously reported results at 2 years and supports that neratinib significantly improves invasive disease-free survival," said principal investigator Arlene Chan, MD, from the Breast Cancer Research Centre at Western Australia and Curtin University in Perth. "One of the purposes of presenting these results at this meeting was to really demonstrate to the oncology community that with

ongoing follow-up — certainly to this point — we are still seeing a consistent benefit of neratinib," she added, explaining that concerns about the persistent benefit of therapy have arisen out of long-term follow-up from the HERA study of patients treated with trastuzumab.

Herceptin Affirmed, Anthracyclines Questioned by Major Trial

With data now out to 10 years, the landmark BCIRG-006 trial of trastuzumab in early-stage HER2-positive breast cancer affirms that the addition of the epoch-making drug significantly improves the efficacy of two standard chemotherapy regimens, compared with chemotherapy alone. The trastuzumab regimens consisted of an anthracycline-containing regimen (doxorubicin [Adriamycin], cyclophosphamide, and docetaxel) and a nonanthracycline-containing regimen (docetaxel and carboplatin). The two are not statistically different from each other in terms of efficacy, compared with chemotherapy alone. However, this equivalent efficacy "comes at a cost" of more congestive heart failure, leukemia, and cardiac dysfunction in the anthracycline group, said lead author Dennis Slamon, MD, PhD, from the University of California, Los Angeles. An expert not involved with the study cautioned that the study was not powered to assess the two regimens. Still, Minetta Lui, MD, from the Mayo Clinic in Rochester, Minnesota, also said the results could result "in a bit of a shift" toward nonanthracycline-containing regimens in this setting.

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