These results are retrospective and provided support to the hypothesis that breast cancer might be biologically different in very young women and the higher likelihood of achieving a pCR in young patients is driven mainly by TNBC subgroup.

Sentinel Lymph Node Biopsy Before or After Neoadjuvant Chemotherapy: Final Results from the SENTINA Trial

Written by Emma Hitt, PhD

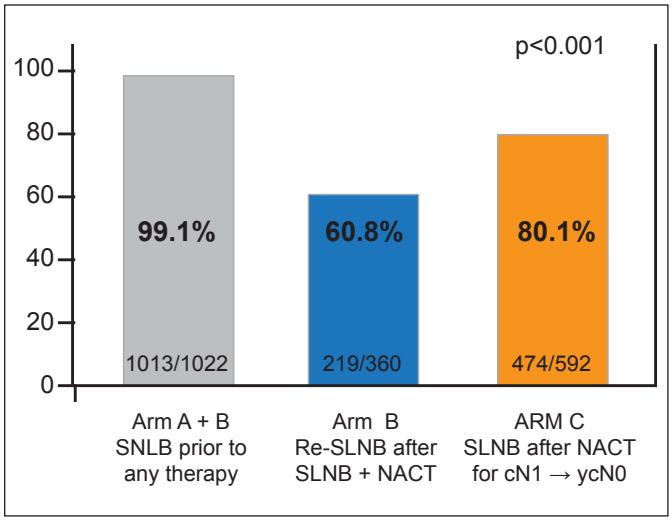
For patients with breast cancer who undergo primary surgery, sentinel lymph node biopsy (SLNB) is the standard staging procedure to determine the axillary status when the patient is clinically node negative [D'Angelo-Donovan DD et al. *Surg Oncol* 2012]. However, for patients who undergo neoadjuvant chemotherapy (NACT), the optimal role and timing of SLNB is still unclear. Thorsten Kuehn, MD, Klinikum Esslingen, Esslingen, Germany, presented final results from the prospective German, multi-institutional Sentinel Neoadjuvant [SENTINA] trial.

The SENTINA trial aimed to evaluate a specific algorithm for the timing of a standardized SLNB procedure and provide data on sentinel lymph node detection rates prior to and after NACT. In addition, the trial assessed false-negative rates for patients who convert from cN1 to cN0 status following chemotherapy and determined factors that might influence detection rates and false-negative rates.

Patients (n=1737) at 103 institutions were distributed among 4 treatment arms according to clinical axillary staging before and after chemotherapy. Arms A and B included patients with cN0 status who underwent SLNB prior to primary systemic therapy. If the sentinel lymph node was negative histologically, no further axillary surgery was performed after primary systemic therapy and the patient was categorized in Arm A. If the sentinel lymph node was positive histologically, a second SLNB and axillary dissection was performed after primary systemic therapy, and the patient was categorized in Arm B. Arms C and D included patients with cN1 status who underwent no axillary surgery prior to primary systemic therapy. Patients who converted to cN0 after primary systemic therapy underwent SLNB and axillary dissection, and were categorized as Arm C; patients who remained cN1 status after primary systemic therapy underwent classical axillary dissection and were categorized as Arm D.

The SLNB detection rate was 99.1% (1013/1022) before primary systemic therapy for Arms A and B, 80.1% (474/592) after primary systemic therapy for Arm C, and 60.8% (219/360) for Arm B after prior SLNB and primary systemic therapy (p<0.001; Figure 1). In Arm B, from 219 patients with a detected sentinel lymph node following primary therapy, 29.2% (64) had a positive axillary status and 70.8% (155) had a negative axillary status. The sentinel lymph node false-negative rate for Arm B was 51.6% (33; 95% CI, 38.7 to 64.2). In Arm C, after primary systemic therapy, 47.7% (226/474) of patients with a detected sentinel lymph node had a positive axillary status and 52.3% (248/474) had a negative axillary status. The sentinel lymph node false-negative rate for Arm C was 14.2% (32 patients; 95% CI, 9.9 to 19.4).

Figure 1. Sentinel Lymph Nodes Detected and Removed.



NACT=neoadjuvant chemotherapy; SLNB=sentinel lymph node biopsy.
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According to Prof. Kuehn, the sentinel lymph node detection rate is excellent for patients who receive SLNB prior to systemic therapy. However, the detection rate for repeated SLNB is "unacceptable." Previous local and systemic treatment significantly impairs the tracer uptake and detection rate. Prof. Kuehn said, "SLNB as a diagnostic procedure is not a reliable tool in patients who convert under neoadjuvant chemotherapy from cN1 to cN0 compared with SLNB in primary surgery."

Chemotherapy Prolongs Survival for Isolated Local or Regional Recurrence of Breast Cancer: The CALOR Trial

Written by Toni Rizzo

Patients who develop isolated local or regional recurrences (ILRR) of breast cancer have a high risk of distant metastasis and death. The only prospective randomized trial of adjuvant chemotherapy in patients with ILRR

reported at >11 years follow-up that patients treated with tamoxifen versus observation had significantly improved disease-free survival (DFS) but no overall survival (OS) advantage [Waeber M et al. *Ann Oncol* 2003]. The Adjuvant Chemotherapy in Treating Women Who Have Undergone Resection for Relapsed Breast Cancer (Chemotherapy as Adjuvant for Locally Recurrent Breast Cancer) [CALOR; NCT00074152] trial, presented by Stefan Aebi, MD, Luzerner Kantonsspital, Lucerne, Switzerland, investigated the impact of chemotherapy on DFS and OS in patients with ILRR. The study had strong participation of the United States National Surgical Adjuvant Breast and Bowel Project, with Irene Wapnir, MD, from Stanford University, Stanford, California, USA, chairing the North American participation.

Patients with a first ILRR excised with negative or microscopically involved tumor margins and no evidence of tumor in supraclavicular lymph nodes or distant metastasis were eligible for the trial. After surgery, patients were stratified according to prior chemotherapy, estrogen receptor (ER) and/or progesterone receptor (PR) status, and location of ILRR; they were then randomized to treatment with chemotherapy (n=85) or no chemotherapy (n=77). Patients with hormone receptor-positive cancers also received endocrine therapy, and those with human epidermal growth factor receptor 2 (HER2)-positive cancers could receive HER2-directed therapy. The specific chemotherapy was chosen by investigators, but a 2-drug regimen for 3 to 6 months was recommended. Radiation therapy at ≥40 Gy was required for patients with microscopically involved margins and recommended for all patients. The primary endpoint was DFS and the secondary endpoint was OS.

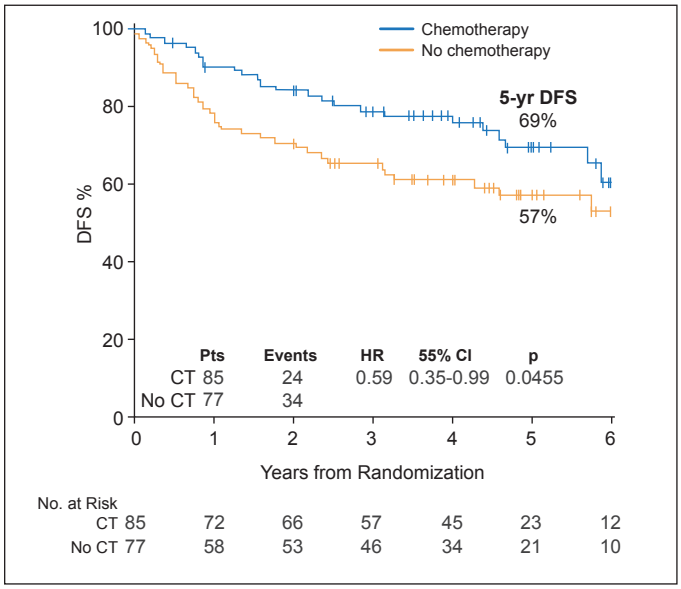
Baseline characteristics were well balanced between the 2 groups. Therapies for ILRR received by patients in the chemotherapy versus no chemotherapy arms were radiation therapy (44% vs 39%), luteinizing hormone-releasing hormone (6% vs 13%), fulvestrant (0% vs 1%), tamoxifen (18% vs 18%), aromatase inhibitors (55% vs 53%), endocrine treatment for ER-positive ILRR (91% vs 92%), and HER2-directed therapies (7% vs 5%). Patients in the chemotherapy arm were treated with monotherapy (docetaxel or paclitaxel [20%], or capecitabine [11%]) or polychemotherapy (anthracycline-based [48%], anthracycline plus taxane-based [1%], or taxane-based [16%]). Therapies for ILRR in the chemotherapy arm are shown in Table 1.

At a median follow-up of 4.9 years, patients in the chemotherapy group versus the no-chemotherapy group had significantly improved DFS (69% vs 57%; HR, 0.59; 95% CI, 0.35 to 0.99; p=0.0455; Figure 1) and OS (88% vs 76%; HR, 0.41; 95% CI, 0.19 to 0.89; p=0.02).

Table 1. Therapies for ILRR in the Chemotherapy Arm.

	Chemotherapy (n=85)
Monotherapy	31%
Docetaxel or paclitaxel	20%
Capecitabine	11%
Polychemotherapy	69%
Anthracycline-based	48%
Anthracycline plus taxane-based	1%
Taxane-based	16%

Figure 1: DFS with Chemotherapy Versus No Chemotherapy.



CT=chemotherapy; DFS=disease-free survival; Pts=patients.
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On multivariate analysis controlling for ILRR location, disease-free interval, ER status, and prior adjuvant chemotherapy, the results remained significant for both DFS (HR, 0.50; p=0.01) and OS (HR, 0.37; p=0.02).

Analysis by ER status showed a significant difference in DFS with chemotherapy versus no chemotherapy in ER-negative patients (DFS, 67% vs 35%; HR, 0.32; 95% CI, 0.14 to 0.73; p=0.007) but not in ER-positive patients (70% vs 69%; HR, 0.94; 95% CI, 0.47 to 1.89; p=0.87).

In the CALOR trial, adjuvant chemotherapy reduced the risk of DFS events by 41% and death by 59%. The authors concluded that adjuvant chemotherapy should be recommended for patients with completely resected isolated local or regional recurrences. The results are strongest for patients with ER-negative recurrences. Longer follow-up is needed for patients with ER-positive recurrences.