0.81; 95% CI, 0.69 to 0.96; nominal p=0.016 [cannot be claimed as statistically significant]).

Serious adverse events (SAEs) were reported in 9.7% of patients taking fulvestrant 500 mg and 7.2% of those taking fulvestrant 250 mg. Treatment-related SAEs were reported in 2.2% of patients receiving 500 mg versus 1.1% receiving 250 mg. SAEs resulting in death during the whole treatment period occurred in 1.5% receiving 500 mg versus 2.0% receiving 250 mg.

Consistent with the previously reported PFS and OS data, the final OS analysis at 75% maturity showed that fulvestrant 500 mg is associated with a 4.1-month increase in median OS and a 19% reduction in the risk of death compared with fulvestrant 250 mg. Analysis of the first subsequent therapies does not support an imbalance between the 2 study arms. Only 2% of patients crossed over from 250 to 500 mg. However, activity for 500 mg after pretreatment with 250 mg is unknown. The safety results do not support a clinically relevant difference between fulvestrant 250 and 500 mg, and are consistent with the previously reported safety profile of fulvestrant 500 mg.

Neoadjuvant Chemotherapy in Women 35 and Under

Written by ***Emma Hitt, PhD***

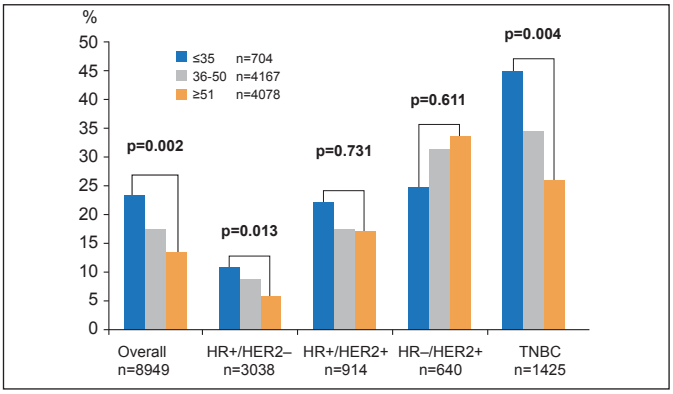
Evidence suggests that breast cancer in younger women may be clinically and etiologically distinct from older women [Bleyer A et al. *Nat Rev Cancer* 2010]. Breast cancer in young women demonstrates a worse prognosis and a more aggressive phenotype, higher proportions of high-grade and later-stage tumors, lower estrogen receptor (ER) positivity, and, in some studies, higher expression of human epidermal growth factor receptor 2 (HER2) [Bleyer A et al. *Nat Rev Cancer* 2010; Gnerlich JL et al. *J Am Coll Surg* 2009]. While some studies point to a unique breast cancer biology in young women, others have illustrated that the aggressive nature is the result of higher frequencies of aggressive breast cancer subtypes among younger patients. Sibylle Loibl, MD, PhD, German Breast Group, Neu-Isenburg, Germany, presented data on the response to neoadjuvant chemotherapy in women with breast cancer who are aged ≤35 years compared with older women.

The meta-analysis included 8949 patients with operable or locally advanced nonmetastatic breast cancer from 8 neoadjuvant German studies with follow-up. Patients were categorized into 3 age groups: ≤35 (n=704), 36 to 50 (n=4167), and ≥51 years (n=4078). All patients with endocrine responsive disease received adjuvant endocrine therapy. Subgroup analyses were conducted defined by hormone receptor (HR) and HER2 status.

Breast cancer subtype distribution was found to differ according to patient age group. Triple-negative breast cancer (TNBC) was more common in patients aged ≤35 than patients aged >35 years (26% vs 19%). In contrast, HR-positive/HER2-negative breast cancer was more common in patients aged >35 years compared with patients aged ≤35 years (37% vs 29%). HER2-positive tumors were similar in both age groups regardless of HR status.

The overall pathologic complete response (pCR) rate (defined as ypT0, ypN0) was significantly higher in patients aged ≤35 compared with patients aged ≥51 years (23% vs 13%; p=0.002; Figure 1). The only subgroups with pCR rates that were statistically higher for patients aged ≤35 years compared with patients aged ≥51 years were HR-positive/HER2-negative (11% vs 6%; p=0.013) and TNBC (45% vs 25%; p=0.004).

Figure 1. pCR Rates Overall and in Subgroups.



*HR and HER2-status not available for all patients. HER2=human epidermal growth factor receptor 2; HR=hormone receptor; TNBC=triple-negative breast cancer.
Reproduced with permission from S Loibl, MD, PhD.

The pCR rate was an independent predictor of disease-free survival (DFS) when the analysis was adjusted for age, tumor size, nodal status, histological type, grading, and clinical trial. DFS was significantly inferior in patients aged ≤35 compared with patients in the 36 to 50 (p=0.031) and the ≥51 year age groups (p=0.022). The difference was greater between age groups in patients who did not achieve pCR; patients aged ≤35 years had a 25% higher risk of relapse compared with the 36 to 50 (p=0.002) and ≥51 year age groups (p=0.001). In contrast to previous studies, patients aged ≤35 years with HR-positive/HER2-negative breast cancer who achieved a pCR had a better DFS compared with patients in the same age group who did not achieve pCR. Local recurrence-free survival was also significantly inferior in patients aged ≤35 years compared with patients in the 36 to 50 (p=0.017) and ≥51 years age groups (p=0.00018). Overall survival was not significantly different between the 3 age groups.

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

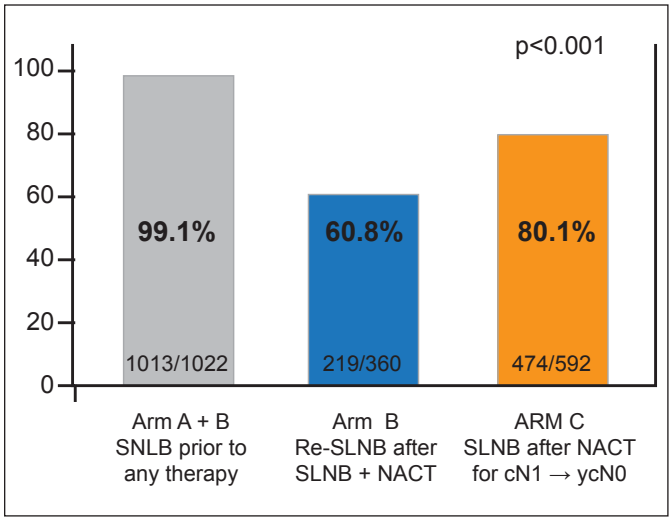
For patients with breast cancer who undergo primary surgery, sentinel lymph node biopsy (SLNB) is the standard staging procedure to determine the axillary status when the patient is clinically node negative [D'Angelo-Donovan DD et al. *Surg Oncol* 2012]. However, for patients who undergo neoadjuvant 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