

Neoadjuvant chemotherapy (NACT) for estrogen receptor negative and HER2 normal breast cancer (DNBC) in Denmark

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INTRODUCTION

NACT has been introduced to facilitate less invasive surgery and to obtain better prognostication and guidance regarding post neoadjuvant therapy. Here we describe the outcome from NACT in an unselected Danish cohort of DNBC regarding pCR, node-conversion, and surgical procedure.

DBCG was established in 1976 and have since maintained a clinical database for early breast cancer patients in Denmark. Data on diagnosis, treatment and follow-up have been systematically and prospectively collected.

Receptor negative breast cancers were characterized by:
1. Less than 1% estrogen receptor (ER) positive cells or < 10% ER+ cells and either < 10% progesterone positive cells or a non-luminal PAM50 subtype
2. Normal HER2 expression (0 or 1+) and/or absence of HER2 amplification.

METHODS

This study is a retrospective nationwide cohort-study based on real-world data. Before initiation of NACT eligible patients diagnosed between 1/1-2016-31/12-2019 were prospectively registered in the Danish Breast Cancer Group clinical database. Exclusion criteria were LABC, defined as mastitis carcinomatosa/inflammatory breast cancer, inoperable breast cancer, ulcerating breast cancer or infra clavicular lymph node metastasis, primary metastatic disease or prior malignancy. In total 484 patients were included and examined according to pre- and post-NACT characteristics, surgical procedure and chemotherapy. pCR was defined as no residual invasive tumor in the breast or in the axillary lymph nodes (ypT0/Tis ypN0(-)). Patients were allocated to either 3+3 or 4+4 series with epirubicin and cyclophosphamide (q3w) followed by a taxane (docetaxel (q3w) or weekly paclitaxel). Capecitabine was recommended after neoadjuvant therapy for patients who did not receive pCR during prior chemotherapy, depending on comorbidities. Standard chemotherapy doses as listed in figure 1.

Chemotherapy standard doses:

Cyclophosphamide: 600 mg/m²
Epirubicin: 90 mg/m²
Paclitaxel: 80 mg/m²
Docetaxel: 100 mg/m²
Capecitabine: 1000 mg/m²

Figure 1: standard chemotherapy doses.

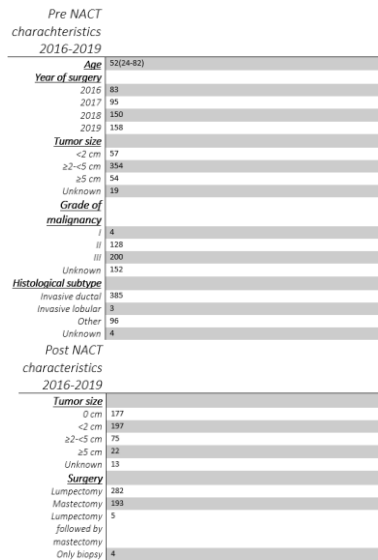


Table 1: Baseline characteristics and post NACT characteristics

RESULTS

Median age was 52 years (range 24-82). Pre-NACT tumor size was divided into 3 groups, 0-2 cm (11.8%), 2-5 cm (73.1%) and 5 cm or larger (11.2%). Patients were allocated to receive 3+3 (49%) or 4+4 (37%) series of chemotherapy depending on tumor size. The remaining 14% received another combinational chemotherapy regimen. Overall, 156 (32.2%) achieved pCR (Table 2). Among patients with biopsy verified node-positive pre-NACT 50% had tumor-free axillary nodes post-NACT (Table 2). The majority received breast conserving surgery (BCS; 58% or mastectomy (40%) and in 2% definitive surgery was unknown (Table 1). In the group not achieving pCR, 20% received post-neoadjuvant capecitabine.

| | POST NACT axillary lymph nodes | | | | | Total |
|------------------------------|--------------------------------|------------------|-----|----------------|---------|-------|
| | Macro-metastasis | Micro-metastasis | ITC | No tumor cells | Unknown | |
| PRE NACT Lymph node positive | 61 | 7 | 4 | 73 | 2 | 147 |
| Lymph node negative* | 26 | 8 | 12 | 271 | 20 | 337 |
| Total | 87 | 15 | 16 | 344 | 22 | 484 |
| Miles-Payne Response | | | | | | |
| 1 | 6 | 5 | 6 | 156 | 4 | 177 |
| 2 | 18 | 7 | 2 | 49 | 1 | 77 |
| 3 | 31 | 1 | 3 | 72 | 2 | 109 |
| 4 | 28 | 2 | 5 | 55 | 1 | 91 |
| Unknown | 4 | 0 | 0 | 12 | 14 | 30 |
| Total | 87 | 15 | 16 | 344 | 22 | 484 |

Table 2: Treatment response after neoadjuvant therapy. *includes patients with a negative fine needle aspiration and those who were clinically negative.

CONCLUSION

Surgery was reduced in more than half of the patients either by converting mastectomy to BCS or by avoiding axillary dissection. However, only 32.9% achieved a pCR and consequently we will in the future consider more effective chemotherapy regimens.