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Speaker: William W. Thomassen,
william.wendler.thomassen@regionh.dk

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

William Wendler[1,2], Tobias Berg[1,2], Maj-Britt Jensen[1] and Bent Ejlertsen[1,2]

[1]Danish Breast Cancer Group (DBCG), Rigshospitalet, Copenhagen University Hospital, Copenhagen
[2]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen

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 carcinomatosis/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(i-)).
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 figure1.

Chemotherapy standard doses:

Cyclophosphamide: 600mg/m^2
Epirubicin: 90 mg/m^2
Paclitaxel: 80 mg/m^2
Docetaxel: 100 mg/m^2
Capecitabine:1000 mg/m^2

Figure 1: standard chemotherapy doses.

Pre NACT charachteristics 2016-2019	
Age	52(24-82)
Year of surgery	
2016	83
2017	95
2018	150
2019	158
Tumor size	
<2 cm	57
≥2-<5 cm	354
≥5 cm	54
Unknown	19
Grade of malignancy	
I	4
II	128
III	200
Unknown	152
Histological subtype	
Invasive ductal	385
Invasive lobular	3
Other	96
Unknown	4
Post NACT characteristics 2016-2019	
Tumor size	
0 cm	177
<2 cm	197
≥2-<5 cm	75
≥5 cm	22
Unknown	13
Surgery	
Lumpectomy	282
Mastectomy	193
Lumpectomy followed by mastectomy	5
Only biopsy	4

Table 1: Baseline characteristics and post NACT characeteristics

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.

N =484	POST NACT axillary lymph nodes					
	Macro-metastasis	Micro-metastasis	ITC	No tumor cells	Unknown	Total
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
Miller-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.

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