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# Oncologic safety of breast conserving surgery after tumor downsizing by neoadjuvant therapy: A retrospective single centre cohort study

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## Abstract

**Objective**: The objective of this study is to analyse local recurrence rates in patients receiving neoadjuvant Chemotherapy (nCT) comparing mastecomized (MX) patients with those undergoing breast conserving therapy (BCT). **Method**: Patients undergoing breast cancer surgery after nCT (3xCMF or 3-6xED) between 1995 and 2007 at our department were retrospectively analysed. **Results**: The median follow up was 60 months for 308 patients. Patients who were downsized from MX to BCT with partial or complete response (n=104) had similar local recurrence free survival (LRFS) compared to patients who did not experience successful downsizing (n=67) and finally undergoing MX (LRFS MX-BCT 81% versus MX-MX 91%: p=0.79). Uni- and multivariate analyses demonstrated that BCT itself was not an independent prognostic factor for a worse LRFS (p=0.07 and 0.14). After pathologic no change or progressive disease the risk of local recurrence was increased in patients undergoing BCT (MX-BCT; n=6 LRFS 66%) compared with MX (n=44; LRFS 90%; p=0.04). Overall survival in general was better for the BCT group (n=197) compared with MX group (n=111) regardless of clinical response (92% versus 72% p<0.0001). Breast conservation, nodal negativity and low or medium grade histology were prognostic factors for an improved OS (p = 0.02; 0.01; 0.004). **Conclusion**: Our study suggests that BCT is oncologically safe after tumor downsizing by nCT in patients primarily scheduled for mastectomy. These patients, however, should not be treated with breast conservation in the absence of any proven response after nCT.

## Aknowledgement

Florian Fitzal is independent of any commercial funder and he had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

## Introduction

The meta-analysis by Mauri et al [8] with nine randomized prospective trials of 3946 patients comparing neoadjuvant chemotherapy (nCT) with adjuvant therapy demonstrated a significant increased risk for local relapse in the nCT group (RR: 1.22). The inclusion of patients without optimal local treatment after nCT in this meta-analysis, however, was a major bias. A recent Cochrane database review by Mieog et al [10] clearly showed that in prospective randomized trials with adequate local therapy after nCT there is no significant increase in local relapse as compared to primary operation and adjuvant treatment. Patients with adequate local therapy had a significant reduction in local recurrence free survival (LRFS; p=0.02) compared with inadequate local therapy suggesting that breast conserving therapy (BCT) may be safe after nCT.

Prospective studies about BCT after nCT demonstrated a reduced LRFS in patients scheduled for mastectomy before and finally undergoing BCT (MX-BCT) after nCT compared with patients scheduled for BCT before and undergoing BCT (BCT-BCT) after nCT [4-5, 15]. These retrospective subgroup analyses, however, had a major bias as primary cancer biology differs within these two groups. Multivariat analyses have also not been reported. Moreover, patients who are eligible for BCT should not proceed to nCT outside clinical trials as they have no evident benefit so far but might acquire serious side effects from chemotherapy. In this regard,

comparison of oncologic outcome of patients scheduled for mastectomy (MX) but undergoing BCT after nCT (MX-BCT) with those patients scheduled for and undergoing mastectomy after nCT (MX-MX) may be clinically more relevant.

In addition there is no guideline or statement so far regarding the use of BCT after nCT in patients without response to nCT. We hypothesize that those patients should not be treated with BCT as this may in fact increase local relapse.

Thus, the aim of our study in breast cancer patients undergoing nCT due to primarily scheduled mastectomy at a single cancer centre was to compare the oncologic outcome between final mastectomized (MX-MX) and breast conserved patients (MX-BCT) after nCT. Furthermore, we wanted to compare oncologic outcome between clinical responders and non-responders in this respect.

# Patients and Methods

## *Design*

We retrospectively analysed our prospectively build internal patient data base. Data are prospectively entered from a study nurse during each outpatient ward contact into a pre-existing EXCEL work sheet.

## *Inclusion criteria*

All patients who completed nCT and local therapy at the Medical University Vienna from January 1995 up until May 2007 were included in the analyses (n=400). Eligibility for BCT or mastectomy before nCT has been re-evaluated by searching the patients' reports (radiographs, outpatient ward report, operation report). Patients without any clear pre-therapeutic decision for either mastectomy or BCT have been excluded from further analyses (n=75). Patients who were scheduled for BCT before and received MX after neoadjuvant therapy have been eliminated from the final analyses as it was of no interest for our research question (n=17). Thus, data from 308 patients are finally presented.

### *Definition of scheduling patients for mastectomy*

Over the mentioned time period patients were seen by 6 different special breast surgeons dedicating more than 50% of their clinical activity to breast cancer surgery. If the size relation between breast and tumor exceeded 1:4 (more than one breast lump has to be excised) patients were scheduled for mastectomy. Accordingly, multicentricity seen in pretherapeutic radiologic examinations was another factor for scheduling patients for mastectomy before but also after nCT. For primary staging evaluation, clinical assessment as well as mammography and ultrasound or MRI-mammography was mandatory. Restaging was conducted routinely every two to three cycles of therapy.

### *Exclusion criteria*

Metastatic breast cancer

Inflammatory breast cancer

Infiltration of the thoracic wall

ECOG >2

Bilateral breast cancer

Any previous malignancy treated with curative intent and the patient has not been disease-free for 5 years – exceptions are:

- carcinoma in situ of the cervix
- squamous carcinoma of the skin
- basal cell carcinoma of the skin

Any recurrent cancer disease

Pregnant or lactating women

For detailed inclusion and exclusion criteria please refer to [12-14].

## *Cohort groups*

Patients (n=308) were splitted into three groups.

### Group 1 BCT-BCT (n=87)

Patients who were scheduled for BCT before and received BCT after neoadjuvant therapy.

**Group 2 MX-BCT (n=110)**

Patients who were scheduled for MX before but received BCT after neoadjuvant therapy.

**Group 3 MX-MX (n=111)**

Patients who were scheduled for MX before and received MX after neoadjuvant therapy

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We were interested in differences between the three groups with respect to local recurrence free survival (LRFS), overall and distant recurrence free survival (OS, DRFS). Moreover the influence of pathologic response to nCT within the three groups regarding LRFS, OS and DRFS was investigated.

## *Neoadjuvant chemotherapy*

Most patients received neoadjuvant chemotherapy within three prospective randomized trials conducted by the Austrian Breast and Colorectal Cancer Study Group (ABCSG; trials ABCSG-7, ABCSG-14, and ABCSG-24) [12-14].

## ABCSG 7

In ABCSG-7, 423 patients with hormone-receptor negative or high-risk endocrine responsive disease were randomized to three cycles of CMF (cyclophosphamide 600 mg/m², methotrexate 40 mg/m² and 5-fluorouracel 600 mg/m² on days 1 and 8, every four weeks) either as pre- or postoperative treatment. In node-negative patients, another three cycles of adjuvant CMF were administered, whereas node-positive patients received three further cycles of EC (epirubicin 70 mg/m² and cyclophosphamide 600 mg/m² on day 1, every three weeks). Overall response rate to neoadjuvant CMF was 56.2%, with 12 patients (5.9%) achieving pathological complete response (pCR). While no difference in terms of overall survival was observed between the two groups, recurrence-free survival was significantly better in patients receiving chemotherapy postoperatively, leading to the conclusion that three cycles of CMF was insufficient as neoadjuvant chemotherapy [14].

## ABCSG 14

ABCSG-14 compared three cycles of ED (epirubicin 75 mg/m² and docetaxel 75mg/m² on day 1, every three weeks, with granulocyte colony-stimulating factor on days 3 to 10 of each cycle) to six cycles of the same regimen as neoadjuvant treatment for breast cancer.

A total of 292 patients were accrued; six cycles of ED yielded a significantly higher pCR rate (18.6% versus 7.7%; p=0.0045), a significantly higher percentage of patients with negative axillary status (56.6% versus 42.8%; p=0.02), and a trend towards higher rate of breast conserving surgery (75.9% versus 66.9%; n.s.) [12].

**ABCSG 24**

Based upon a proposed synergistic effect of docetaxel and capecitabine, ABCSG-24 compared six cycles of ED plus capecitabine (EDC; epirubicin 75 mg/m² and docetaxel 75mg/m² on day 1, capecitabine 1000 mg/m² BID days1 to 14, every three weeks, plus pegfilgrastim 6 mg on day 2 of each cycle) with standard six cycles of ED as established in ABCSG-14. Patients with Her2-positive disease were also randomized to neoadjuvant trastuzumab every three weeks or control. No results from that second randomization are available yet. A total of 512 patients were accrued to ABCSG-24. Significantly more patients reached pCR with ECD (23.8% versus15.2%; p=0.036), although less patients on ECD completed all six treatment cycles as scheduled, mainly due to capecitabine-associated toxicity [13].

### *Surgery*

4-6 weeks after nCT patients proceeded to surgery. Patients underwent BCT except:

- R1 resection after BCT or initially questionable
- Inflammatory breast cancer
- Multicentric disease (MRI in unclear cases)
- Unwillingness to perform radiotherapy postoperatively
- Good cosmetic outcome after BCT questionable

Non palpable tumors were localized with a hook wire preoperatively. Intra-operative frozen section was done in all cases to determine the resection margins as this reduces the re-operation rate [7, 11]. The resection was done within new resection boundaries after response to nCT in unifocal disease while in multifocal disease resection boundaries were only smaller if all tumors responded to nCT and the total diameter was reduced. Patients with multicentric disease were mastectomized. All patients underwent axillary level I and II dissection except in some selected postmenopausal clinical complete responders with no axillary involvement before nCT who underwent sentinel node biopsy only. However, axillary dissection followed sentinel node biopsy in case of a positive sentinel lymph node.

## *Response evaluation*

### Clinical

Clinical response has been evaluated clinically by palpation and radiologically by mammography and ultrasound or MRI- imaging according to the following criteria:

Clinical complete response (cCR): no radiological and clinical signs of residual disease within the breast and the axilla

Clinical partial response (cPR): radiological and/or clinical signs of residual disease with a diameter <50% of the tumor size before nCT within the breast and/or a positive axilla (palpation)

Clinical no change (cNC): radiological and/or clinical signs of residual disease with a tumor diameter within the range of 25% of the tumor size before nCT

Clinical progressive disease (cPD): radiologic and/or clinical signs of tumor size increase of more than 25% compared to before nCT.

From 2006 onward, MRI-mammography was standard of care for assessment of initial tumour size and treatment response.

## Pathological

Pathologic response has been evaluated from the surgical specimen according to the following criteria:

| | |
|---|---|
| Pathologic complete response (pCRTx$_{\pm is}$N0): | no invasive cancer within the breast lymph node negative |
| Pathologic partial response (pPR): | no invasive cancer within the breast lymph node positive |
| | Invasive cancer within the breast >50% size reduction compared with size before nCT as assessed by mammography and ultrasound or MRI-mammography |
| Pathologic no change (pNC) | invasive cancer within the breast and tumor size increase <25% or decrease <50% compared with clinical size before nCT |
| Pathologic progressive disease (pPD) | invasive cancer within the breast and >25% increase in size or inflammatory breast cancer. |

### *Statistical analyses*

Categorical data is described with absolute and relative frequencies. Chi-square tests are used to test categorical data between groups. In case of sparse data Fisher's exact test was used. Time to event data with respect to LRFS, OS and DRFS are described graphically by the method of Kaplan-Meier and tested between groups by the log-rank test. The proportional hazards regression model of Cox was used to model the prognostic value of covariates in a uni- and multivariate manner.

All p-values are two-sided and $p \leq 0.05$ were considered significant. All calculations are performed with the statistical software SAS® (Version 9.2, SAS Institute Inc., Cary, NC, USA).

## Results

### *Demographic data*

From the 308 patients 221 were scheduled for mastectomy before nCT. 111 patients had to be mastectomized and 110 underwent BCT after nCT while 87 patients were scheduled for and received BCT after nCT. Primary level I axillary dissection was conducted in 273 patients, Sentinel only in 7 patients (clinical negative lymph nodes and good response, pathologic negative sentinel node) and

sentinel and axillary dissection in 28 patients. All patients had at least 1mm free margin and underwent postoperative radiotherapy with a boost.

Table 1 shows the demographic data of the groups and compares between all patients finally mastectomized (MX) with those finally undergoing BCT. Table 1 also compares between MX-MX and MX-BCT and between BCT-BCT and MX-BCT. Preoperative clinical and postoperative pathologic tumor size were significantly different between patients undergoing MX and BCT while there was no difference in tumor size between BCT-BCT and MX-BCT patients after nCT. Lymph node status differed significantly between the groups while menopause, endocrine responsiveness (any receptor positive) and grading did not differ between the groups.

## *Oncologic outcome*

The median follow up period was 60 months.

### Local recurrence free survival

Comparing all patients finally mastectomized (n=111) with patients undergoing breast conservation after nCT (n=197) there was no significant difference between the two groups regarding local recurrence free survival (5years: 91% versus 89%; p=0.92). Within all

patients who were initially scheduled for mastectomy an showing pathologic response (partial or complete remission), there was no increase of local relapse in those finally undergoing BCT after nCT compared with those finally undergoing mastectomy after nCT as shown in figure 1. Analyzing local relapse within pathological non responders, patients finally undergoing BCT, however, showed a significant increased risk in local recurrence as shown in figure 2. Comparing patients with pathologic response who were scheduled for mastectomy and finally receiving BCT (n=104) with patients who were primarily scheduled for and finally received BCT (n=69) the local recurrence free survival was only marginal significant different in favour of the BCT-BCT group (5-years: 84% versus 97% p=0.046).

**Overall and distant free survival**

Patients finally undergoing BCT (n=197) had an improved overall and distant recurrence free survival compared with patients finally mastectomized (n=111) regardless of response (5 years-OS: 92% versus 74%; 5 years-LRFS: 81% versus 58% p<0.0001). Patients who showed a pathologic response to nCT and were scheduled for mastectomy had an increased overall survival if breast conservation was performed at last as shown in figure 3. This was similar for LRFS (78% versus 61% p=0.052). There was no difference in 5 years-OS or LRFS comparing patients with pathologic response who were scheduled for mastectomy and finally

receiving BCT (n=104) with patients who were primarily scheduled for and finally received BCT (n=69; OS: 89% versus 96% p=0.27; LRFS: 78% versus 89% p=0.10)

### Prognostic factors for OS, LRFS and DRFS

Univariate and multivariate analyses as shown in table 2 revealed that BCT (both MX-BCT and BCT-BCT versus MX-MX), nodal negativity and grade 1 or 2 were prognostic for an improved OS (table 2). There were no prognostic factors for LRFS within these patients (table 3) while ductal type, smaller pathologic tumor size, grade 1 and 2 as well as nodal negativity were prognostic factors for a better DRFS (not shown).

## Discussion

Our retrospective analysis shows that BCT after nCT does not increase the risk for LRFS compared with MX while OS as well as DRFS were significantly improved in BCT patients independent of their response to nCT. Patients who were scheduled for MX but finally underwent BCT due to clinical response showed no significant difference in LRFS compared with patients finally undergoing MX. Subgroup analyses with non-responders (pathologic no change or progressive disease), however, revealed a significant

increased risk of local relapse after BCT compared with MX in this specific group. Multivariate analyses show that BCT is not a significant prognostic factor for reduced LRFS or DRFS but predicted for superior OS.

The first publications of prospective nCT trials suggested an increased risk for death and local relapse for patients undergoing BCT after nCT. Published data from the EORTC 10920 trial suggested that there may be a reduction of OS in patients scheduled for mastectomy comparing with patients scheduled for BCT finally undergoing BCT after nCT (HR=2.53) [15]. However, pre-therapeutic lymph node status differed between the groups (BCT-BCT 54% cN1 versus MX-BCT 64% cN1) possible influencing the final result. Similar data from the NSABP-B18 trial demonstrated a reduced LRFS in MX-BCT patients compared with BCT-BCT patients (15.9% versus 9.9%) [17]. However, after controlling for patient age and clinical tumor size before treatment that difference was not significant any more [17]. Moreover tamoxifen has been shown to reduce LRFS [3] and all patients regardless of receptor status received tamoxifen in NSABP-B18.

Our analyses support the hypothesis that LRFS within the group of patients finally receiving BCT after nCT is worse in patients scheduled for mastectomy compared with patients scheduled for BCT before nCT. The difference was still significant after excluding non-responders (all patients after nCT with no change or progressive disease). Clinical and pathological tumor size as well as grading, however, differed significantly while nodal status, menopause and endocrine responsiveness did not differ between these two groups.

Thus, we suggest that the difference in LRFS seen in our study as well as in other prospective trials is biased due to different tumor stage and should not lead to any contraindication for BCT after nCT.

Moreover patients scheduled for BCT should only be treated with nCT in prospective randomized trials as there is no proven benefit for this group [7, 13]. The advantage of achieving pCR after nCT and thus, of knowing the response of the tumor to a certain kind of drug, is certainly a promising treatment guidance. However, pCR should only be used as surrogate marker in clinical trials. In addition, selecting patients with smaller sized breast cancer who are eligible for BCT in neoadjuvant trials may increase the number of patients receiving unnecessary chemotherapy as the use of nCT never improved oncologic outcome [10]. Thus, the surgical question regarding standard nCT outside clinical trials is, whether BCT after downsizing breast cancer in patients scheduled for mastectomy is oncologic safe. This group (MX-BCT) has never been compared with patients needing MX after planned MX (MX-MX).

Our retrospective analyses may in part answer this issue showing that patients after tumor downsizing primarily scheduled for MX but finally undergoing BCT after nCT had no increase in local relapse compared with patients scheduled for and finally undergoing MX. Only patients who showed no response to nCT undergoing BCT had a significant increased local relapse rate compared with MX patients. Due to a significant difference in nodal status, grading and tumor size within these two groups the results have to be discussed with caution. However, multivariate analyses for OS, LRFS and DRFS show that BCT is no independent predictive factor for

LRFS and DRFS supporting the hypothesis that breast conservation is safe after tumor downsizing by nCT. A prospective evaluation is needed to further elucidate this issue.

A meta-analyses published in 2005 [8] including 9 randomized studies comparing pre- with postoperative chemotherapy in 3946 patients demonstrated a reduced LRFS in the BCT group after nCT compared with patients undergoing BCT and adjuvant therapy. This difference was largely influenced by the trials in which surgery was omitted and local treatment was achieved with the use of radiotherapy only in several patients [1, 9]. A Cochrane analysis of 14 prospective studies with 5500 patients comparing pre- with postoperative chemotherapy demonstrated similar LRFS within the BCT group in trials with adequate local therapy (including surgery in all patients) while inadequate local therapy (radiotherapy only in several patients) resulted in a significant worse LRFS [10] supporting our results.

Published guidelines [2, 6, 16] suggested to omit BCT in patients with a high probability of local recurrence (N2 or N3, T >2cm, lymphovascular invasion, multifocal disease, young age). While our study showed that these parameters were no independent predictors for LRFS except clinical response, we suggest including the latter into surgical decision making rather than other factors.

Major drawback of the study is that patients who were scheduled for mastectomy but finally underwent BCT showed significant smaller tumors compared with mastectomized patients. This may bias our finding that local recurrence is not increased in patients undergoing BCT after nCT and tumor downsizing as size increase the risk for local relapse. This heterogeneity is a result of subjective pre-therapeutic allocation to primary mastectomy before nCT by the treating physician. However, so far this is the only retrospective analyses of more than 300 patients analysing true cancer downsizing and local recurrence rate comparing mastectomy and final BCT. Prospective studies have to further investigate this hypothesis. It is also interesting to see that 56 patients underwent mastectomy though a clinical T1/2 staging. The reason is a high rate of additional extensive intraductal components (n=48) necessitating mastectomy and the fact that 8 patients had a very small breast and BCT would have resulted in an inferior cosmetic result.

In conclusion our study suggests that BCT is safe after tumor downsizing and pathologic response by nCT independent of the initial nodal stage and tumor size. Patients scheduled for mastectomy should not be treated with breast conservation in the absence of any proven response to nCT.

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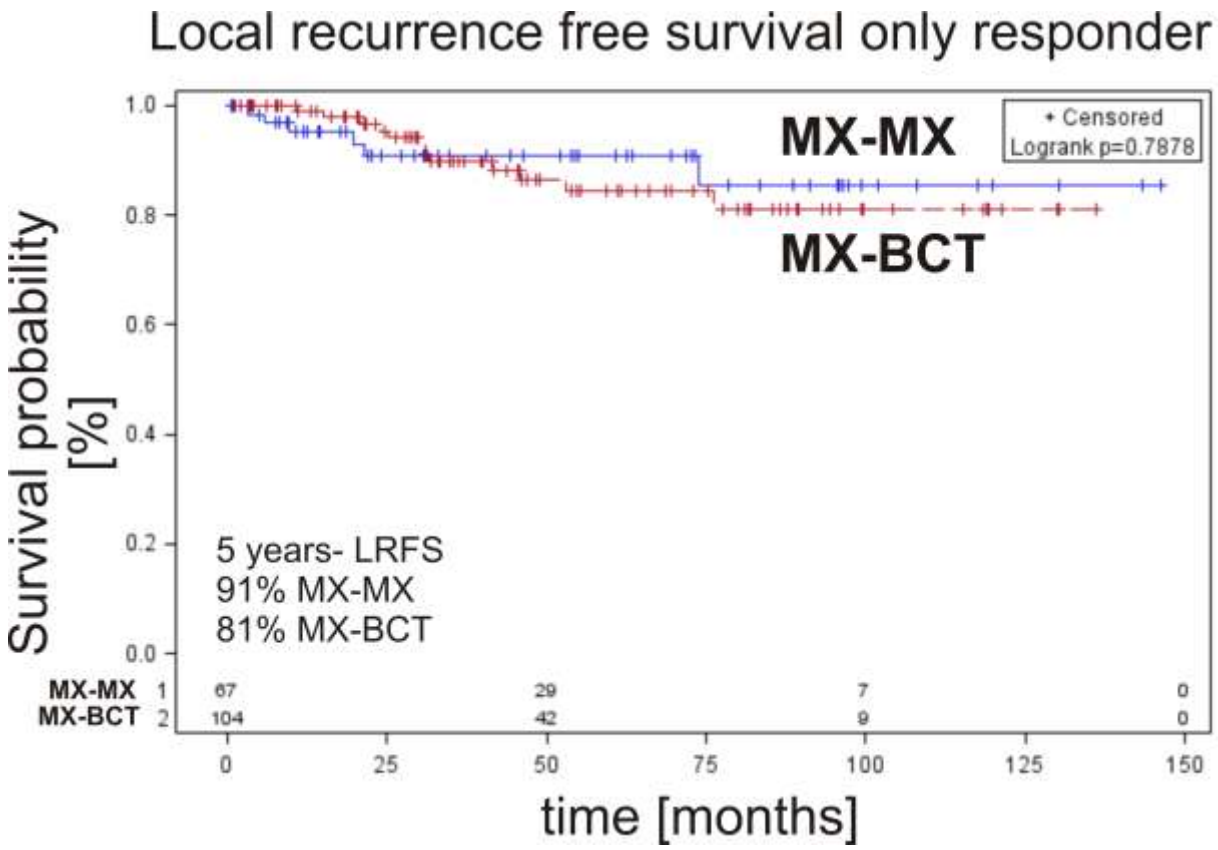
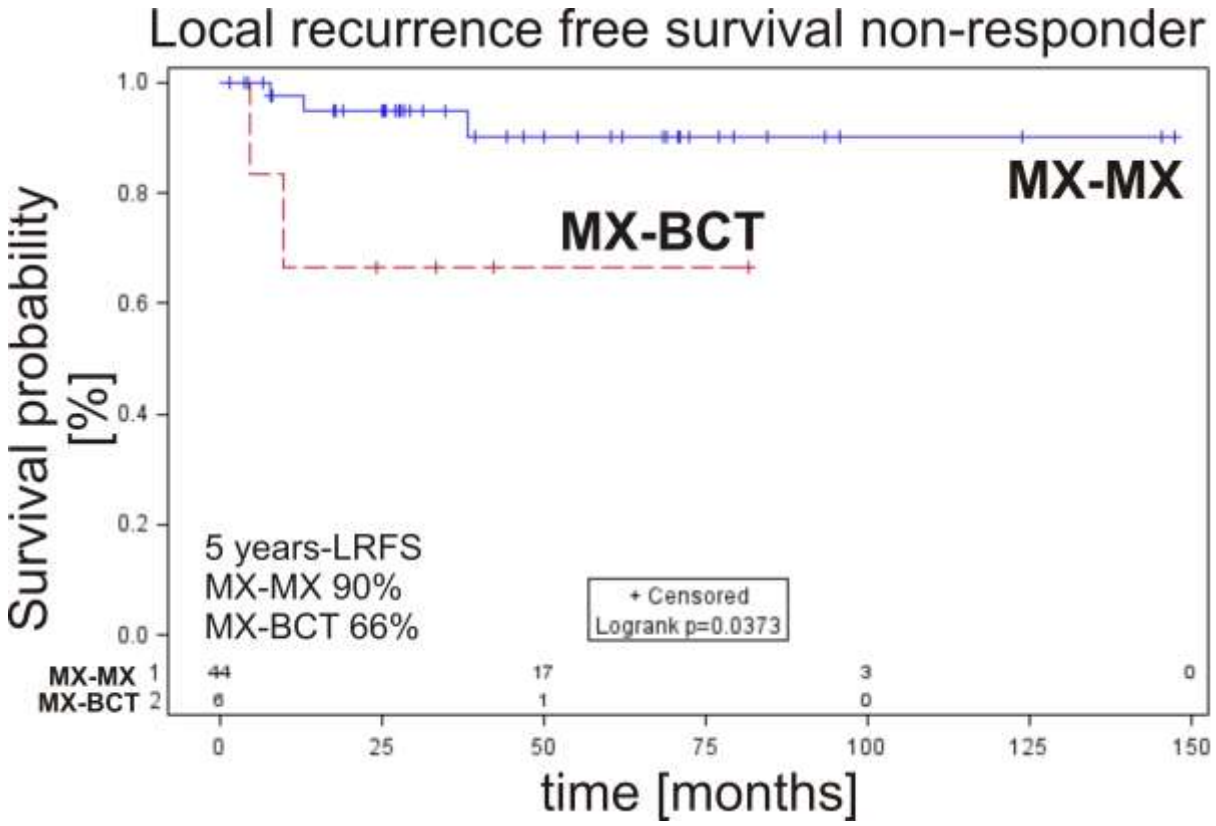
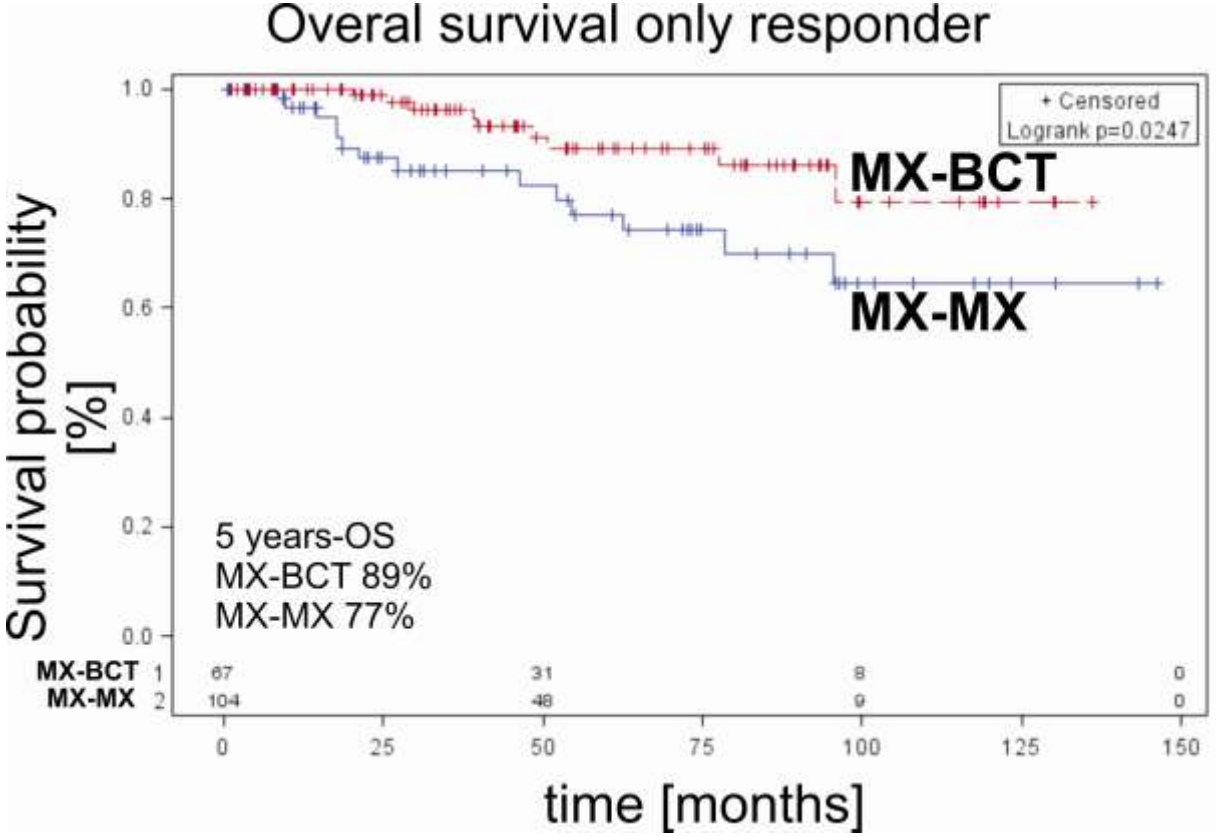

Local recurrence free survival only responder
Survival probability [%]
1.0
0.8
0.6
0.4
0.2
0.0
MX-MX
MX-BCT
+ Censored
Logrank p=0.7878
5 years- LRFS
91% MX-MX
81% MX-BCT
MX-MX 1 67 29 7 0
MX-BCT 2 104 42 9 0
0 25 50 75 100 125 150
time [months]


Local recurrence free survival non-responder
Survival probability [%]
1.0
0.8
0.6
0.4
0.2
0.0
MX-MX
MX-BCT
5 years-LRFS
MX-MX 90%
MX-BCT 66%
+ Censored
Logrank p=0.0373
MX-MX 1 44 17 3 0
MX-BCT 2 6 1 0
0 25 50 75 100 125 150
time [months]




| | percentage | | p | percentage | | p | percentage | | p |
|---|---|---|---|---|---|---|---|---|---|
| Group | **BCT** | **MX** | $X^2$ | **MX-BCT** | **MX-MX** | $X^2$ | **BCT-BCT** | **MX-BCT** | $X^2$ |
| n = 308 | 197 (64%) | 111 (36%) | | 110 (36%) | 111 (36%) | | 87 (28%) | 110 (36%) | |
| **clinical tumor size before surgery** | | | | | | | | | |
| cT1/2 (before neoadjuvant) | 73 | 24 | | 54 | 24 | | 97 | 54 | |
| cT3/4 (before neoadjuvant) | 27 | 76 | <0.001 | 46 | 76 | <0.001 | 3 | 46 | <0.001 |
| cT1/2 (after neoadjuvant) | 98 | 56 | <0.001 | 98 | 56 | <0.001 | 99 | 98 | 0.837 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| cT3/4 (after neoadjuvant) | 2 | 44 | | 2 | 44 | | 1 | 2 | |
| **pathologic response** | | | | | | | | | |
| pCR Tx±isN0 (no invasive but in situ Ca) | 11 | 3 | | 10 | 3 | | 11 | 10 | |
| pCR Tx±isN1 (no Ca in breast/axillla positive) | 3 | 5 | | 3 | 5 | | 2 | 3 | |
| pPR | 75 | 52 | | 82 | 52 | | 66 | 82 | |
| pNC/PD | 12 | 40 | <0.001 | 5 | 40 | <0.001 | 21 | 5 | 0.008 |
| **TNM** | | | | | | | | | |
| pT0is/1/2 | 96 | 48 | | 94 | 48 | | 100 | 94 | |
| pT3/4 | 4 | 52 | <0.001 | 6 | 52 | <0.001 | 0 | 6 | 0.038 |
| G3 | 47 | 50 | | 54 | 50 | | 38 | 54 | |
| G1/2/x | 53 | 50 | 0.777 | 46 | 50 | 0.734 | 62 | 46 | 0.033 |
| N0 | 58 | 25 | | 55 | 25 | | 63 | 55 | |
| N1 | 42 | 75 | <0.001 | 45 | 75 | <0.001 | 37 | 45 | 0.314 |
| **Menopause** | | | | | | | | | |
| prae | 45 | 38 | | 41 | 38 | | 51 | 41 | |
| post | 55 | 62 | 0.389 | 59 | 62 | 0.742 | 49 | 59 | 0.202 |
| **endocrine responsive** | | | | | | | | | |
| non-responsive (ER/PgR neg) | 40 | 41 | | 47 | 41 | | 30 | 47 | |
| endocrine responsive (any positive Er/Pr) | 60 | 59 | 1.000 | 53 | 59 | 0.461 | 70 | 53 | 0.461 |

**Table 2**

| **prognostic factor for overall survival** | | univariate | multivariate | prognostic variable |
|---|---|---|---|---|
| **Surgical group** | **MX-MX vs. MX-BCT vs BCT-BCT** | **0.0001** | **0.02** | **BCT** |
| **clinical response** | CR versus PR/NC/PD | 0.36 | 0.52 | |
| **pathological response** | CR versus PR/NC/PD | 0.09 | 0.99 | |

| | | | | |
|---|---|---|---|---|
| **tumor type** | ductal versus lobular | **0.04** | 0.10 | |
| **pathological tumorsize** | pT0/1/2 versus pT3/4 | **0.04** | 0.84 | |
| **menopausal status** | praemenopausal vs. postmenopausal | 0.90 | 0.67 | |
| **lymph node status** | **neg versus pos** | **0.0006** | **0.01** | **N0** |
| **endocrine responsive** | Er/Pr neg versus any other | **0.03** | 0.09 | |
| **her2neu** | pos versus neg | 0.61 | 0.68 | |
| **grading** | **G3 versus G1/2** | **0.002** | **0.004** | **G1/2** |

MX-MX: patients scheduled for mastectomy and receiving mastectomy after neoadjuvant therapy
MX-BCT: patients scheduled for mastectomy but receiving breast conserving therapy after neoadjuvant therapy
BCT-BCT: patients scheduled for breast conservation and receiving breast conservation after neoadjuvant therapy
CR: complete response; PR: partial response; NC: no change; PD: progressive disease

**Table 3**

| **prognostic factors for local recurrence** | | univariate | multivariate |
|---|---|---|---|
| **Surgical group** | MX-MX vs. MX-BCT vs BCT-BCT | 0.07 | 0.11 |
| **clinical response** | CR/PR versus NC/PD | 0.86 | 0.89 |
| **pathological response** | CR versus PR/NC/PD | 0.51 | 0.51 |
| **tumor type** | ductal versus lobular | 0.08 | 0.09 |
| **pathological tumorsize** | pT0/1/2 versus pT3/4 | 0.96 | 0.76 |
| **menopausal status** | praemenopausal vs. postmenopausal | 0.64 | 0.64 |

| | | | |
|---|---|---|---|
| **lymph node status** | neg versus pos | 0.46 | 0.48 |
| **endocrine responsive** | Er/Pr neg versus any other | 0.08 | 0.27 |
| **her2neu** | pos versus neg | 0.99 | 0.91 |
| **grading** | G3 versus G1/2 | 0.34 | 0.92 |

MX-MX: patients scheduled for mastectomy and receiving mastectomy after neoadjuvant therapy
MX-BCT: patients scheduled for mastectomy but receiving breast conserving therapy after neoadjuvant therapy
BCT-BCT: patients scheduled for breast conservation and receiving breast conservation after neoadjuvant therapy
CR: complete response; PR: partial response; NC: no change; PD: progressive disease