between MX-BCT and BCT-BCT ($p = 0.04$) while there was no significant difference when comparing MX-MX versus MX-BCT patients ($p = 0.79$). Multivariate analyses using surgical group, menopause, lymph node status, grading, pathological response, tumor type, endocrine responsiveness and her2neu status demonstrated no influence of any of these parameters on LRFS. Surgical group (BCT), lymph node status (N0) and grading (G1/2) were predictive for OS while tumor type (ductal), lymph node status (N0) and grading (G1/2) were predictive for DRFS.

Conclusion: There was no significant difference in LRFS, DRFS and OS in patients downsized from mastectomy to breast conservation by neoadjuvant chemotherapy. This was independent of menopause status, endocrine responsiveness, tumor type and pathological response. Thus, BCT is safe after tumor downsizing with neoadjuvant therapy.

MX-BCT: Patient scheduled for mastectomy receiving breast conservation

MX-MX: Patient scheduled for mastectomy receiving mastectomy

BCT-BCT: Patient scheduled for breast conservation receiving breast conservation

LRFS: Local recurrence free survival

DRFS: Distant recurrence free survival

OS: Overall survival

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Intrinsic Susceptibility-Weighted MRI is an effective method of evaluating tumour oxygenation in primary breast cancer and can predict for response to neoadjuvant chemotherapy

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Background: Intrinsic Susceptibility-Weighted MRI (ISW-MRI), also known as Blood oxygenation level dependent (BOLD) MRI, can provide important functional information about whole tumour oxygenation. Higher values of R_2* (the apparent transverse relaxation rate calculated from ISW-MRI data) imply a more hypoxic tumour environment. This study explores the relationships between pretreatment R_2* and tumour characteristics, and assesses whether changes in R_2* correlate with final clinical and pathological response to neoadjuvant chemotherapy (NAC) in breast cancer (BC).

Materials and Methods: 83 pts with primary BC were selected to undergo dynamic contrast-enhanced MRI (DCE-MRI) and ISW-MRI before and after 2 cycles of NAC. Diffusely infiltrating, necrotic or invasive lobular carcinomas (ILC) were excluded due to paradoxical changes in R_2*. DCE-MRI T_1 & T_2-weighted kinetic parameters (K^{trans}, v_e, k_{ep}, $IAUGC_{60}$, relative blood flow (rBF) & volume (rBV), MTT) and R_2* were obtained for whole tumour regions of interest. Relationships between tumour characteristics (grade, size, ER/PR/HER2 status), MRI kinetic parameters and pretreatment R_2* were assessed using Spearman's rank correlation for continuous variables and the Mann-Whitney U test for discrete variables. Pretreatment and changes in R_2* were correlated with final pathological and clinical response to NAC using paired t-testing.

Results: 31 pts (T2−4, N0−2, M0; median age 44, range 22−62) were available for pretreatment and 27 for response assessment. 37 with ILC, ill-defined or necrotic tumours were excluded, 12 did not undergo their first MRI (mainly due to claustrophobia), 1 had only axillary nodal disease visible, 2 had corrupted MRIs that were not analysable and 4 did not have their repeat MRI. 15 pts received anthracycline based NAC and 12 docetaxel NAC. There were no correlations observed between pretreatment R_2* and tumour characteristics or response. Both rBF & rBV were inversely correlated with R_2* ($r = -0.51$, $p = 0.006$; $r = -0.46$, $p = 0.015$), this correlation disappearing with NAC ($r = -0.39$, $p = 0.112$; $r = -0.37$, $p = 0.081$). There were 16 pathological responders & 11 non-responders, and 23 clinical responders & 4 non-responders. Significant R_2* increases were seen with NAC ($34.8s^{-1}$ vs $-31.1s^{-1}$, $p = 0.006$) with larger increases predicting for final pathological ($36.5s^{-1}$ vs $31.7s^{-1}$, $p = 0.025$) and clinical response ($35.5s^{-1}$ vs $31.7s^{-1}$, $p = 0.017$).

Conclusions: Pretreatment R_2* relates to blood rather than tumour oxygenation as suggested by its relationship with blood volume and flow. With the loss of this relationship after NAC, R_2* may become a more reliable marker of actual tumour hypoxia. Furthermore, responders to treatment displayed more hypoxic cancers after 2 cycles of NAC. ISW-MRI has the potential to predict not only therapy response but to identify those who may benefit most from hypoxia targeting agents.

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Applying survival based cost-effectiveness analyses to estimate the impact of patent expiry on the cost-effectiveness of letrozole and anastrozole versus tamoxifen as adjuvant therapy in postmenopausal women with early breast cancer

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Background: The latest update of the BIG 1-98 study (76 months) reports a hazard ratio for overall survival (OS) of 0.83 (95% CI 0.71–0.97) for 5yrs letrozole (LET) vs tamoxifen (TAM) (censoring TAM patients who crossed over to LET). At 100 months, ATAC remains to show a significant OS benefit for anastrozole (ANA) compared to TAM. A new framework for the economic analysis of the aromatase inhibitors (AIs) uses observed differences in OS to estimate the incremental cost per life year (LY), and per quality adjusted LY (QALY) gained of 5 years LET versus 5 years TAM, and 5 years ANA vs 5yrs TAM in ER+ postmenopausal women, from a UK NHS perspective, incorporating possible price reductions due to patent expiry for both AIs.

Methods: Survival probabilities over the 1st 7 years post-surgery were extracted from BIG 1-98, and extrapolated to 20 years using data reported by the Early Breast Cancer Trialists' Group for women receiving 5 years TAM. HRs for LET and ANA were applied to TAM event rates for the first 7 and 9 years, respectively. Conservatively, equivalent annual survival probabilities were assumed thereafter. Reduced ANA costs, to account for generic ANA, were applied from year 1, and reduced LET costs, to account for generic LET, from year 2. Two scenarios were considered for the price of generics; scenario 1 assumed a 50% price reduction and scenario 2 a 70% price reduction. Adverse event (AE) cost and five year costs for locoregional recurrence (LR) and metastases (METS) were also applied. A QALY model applied published utility weights for DFS with AEs, LR, and METS. All costs and health benefits were discounted at 3.5% annually.

Results: For LET, the reference case results show that over a 20 year period, the incremental cost per QALY gained (ICQ) is £9,287, with an upper 95% CI of £32,576. Assuming a 50% price reduction from the 2nd year of treatment lowers the ICQ to £4,727. For ANA, the reference case ICQ is £44,294, with an upper 95% CI of TAM dominating ANA [Table 1]. Assuming a 50% price reduction from the 1st year of treatment lowers the ICQ to £16,099. These results suggest that use of LET is a more cost-effective use of healthcare resource, despite the fact that ANA loss of patent will occur one year prior to LET. The clinical benefits associated with LET far outweigh any cost saving resulting from a lower ANA price for 12 months.

Table 1: Incremental cost per QALY gain for Letrozole and Anastrazole

	Letrozole	Anastrazole
Base case	£9,287	£44,294
Scenario 1: Generics priced 50% below current price	£4,727	£16,099
Scenario 2: Generics priced 70% below current price	£2,902	£3,807

Conclusion: Given the extended follow-up periods for both the ATAC and BIG1−98 trials, one would hope to observe some effect on OS. Using estimates of effects with respect to OS, these new economic analyses suggest a preference for LET, with a lower cost per QALY compared to ANA, despite the shorter time to patent expiry for ANA.

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Factors predicting a pathological complete response following neoadjuvant chemotherapy for breast cancer

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Background: Patients diagnosed with large size or locally advanced breast cancer are frequently treated with neoadjuvant chemotherapy. This work establishes a model, based on demographic and clinicopathological features to predict pathologic complete response (pCR) following neoadjuvant chemotherapy.

Material and Methods: A consecutive group of 335 patients diagnosed with a primary non-metastatic large or locally advanced breast cancer, who had received neoadjuvant systemic therapy between January 2000 and May 2009 at the University Hospitals Leuven was analyzed. After exclusion of 65 patients (58 receiving neoadjuvant hormonal therapy, 4 switching over to neoadjuvant hormonal therapy and 3 refusing operation) 270 patients remained for analysis. pCR was defined as no evidence of invasive tumor in the breast and axillary lymph nodes. Residual in situ lesion without an invasive component is regarded as pCR in this study.