

primary prophylaxis with (pegylated) G-CSF and secondary prophylaxis with epoetin. Pts with tumor reduction less than 50% according to breast ultrasound were randomized to receive either 4 additional cycles TAC or 4 cycles of NX (Vinorelbine 25 mg/m day 1 + 8 plus Capecitabine 2000 mg/m day 1-14, q21(NX). Primary endpoint was sonographic tumor response before surgery. Secondary endpoints were pCR-rate (no invasive/no non-invasive residuals), breast conservation rate, safety and compliance.

Results: Between July 2002 and June 2005 more than 2000 pts were recruited into the GEPARTRIO-trial. Nearly 630 non-responder to TAC \times 2 were randomized to continue TAC or to switch to NX. Median clinical tumor size amounted to 4.0 (1.0–30.0) cm at study entry. Safety and blinded efficacy interim analysis was performed on 154 TAC and 146 NX pts (operable 82.2%, locally advanced 17.8%). Sonographic response before surgery was reported in 67.7%; breast conservation in 59.2% and pCR in 5.2% of these patients. Main toxicities (grade I-IV %TAC vs %NX) were: anemia (92 vs 86), thrombopenia (37 vs 29), neutropenia (72 vs 81), febrile neutropenia (10 vs 6), infection (30 vs 23), vomiting (40 vs 23), diarrhea (44 vs 32), stomatitis (67 vs 45), edema (42 vs 37), asthenia (89 vs 85), hand-foot-syndrome (23 vs 46), allergic (18 vs 21), nail (42 vs 25), dyspnea (35 vs 28), sensory and neuropathy (49 vs 57). Treatment was discontinued in 28 pts (9.3%) due to toxicity (4 vs 7 pts), on patients request (4 vs 8) and tumor progression (4 vs 1).

Conclusions: Ongoing treatment in pts non-responding to TAC \times 2 can achieve sonographic responses in 67% with the chance of breast conservation. Both chemotherapy regimens were well tolerated. NX (without G-CSF) was associated with a better toxicity profile compared to TAC (with G-CSF). The rate of pathologic complete remission was low. Results on the efficacy endpoints will be presented during the meeting.

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Poster

A cost-utility evaluation of adjuvant hormonal options in postmenopausal women with breast cancer: A Belgian perspective

C. Skedgel, D. Rayson, R. Dewar, T. Younis. *Dalhousie University, Medicine, Halifax, Canada*

Background: Based on recent clinical trials, Anastrozole (ANA) for 5 years, Tamoxifen followed by Exemestane for 2.5 years each (TAM-EX) and Tamoxifen for 5 years followed by Letrozole for 3 years (TAM-LET) have become acceptable alternatives to adjuvant Tamoxifen (TAM) for 5 years in postmenopausal (PM) women with hormone receptor positive (HR+) breast cancer. As these newer aromatase inhibitor strategies are associated with both improved disease-free survival and higher drug costs, an economic evaluation was undertaken to compare the relative cost-utility (CU) of ANA, TAM-EX and TAM-LET compared to TAM alone in terms of cost per quality-adjusted life year (QALY) gained.

Methods: A Markov model was developed to calculate cumulative costs and QALYs in a hypothetical cohort of 1000 PM women with HR+ early-stage breast cancer. The baseline event rate and hazard ratios for cancer recurrence and adverse events, including vaginal bleeding, endometrial malignancies, DVT/PE and fractures, were derived primarily from the ATAC, IES and MA17 trials. The primary analysis assumed a carry over benefit for adjuvant therapy beyond the hormonal treatment period. Background mortality rates were taken from Belgian life tables. Costs of hormonal therapies, breast cancer management, and adverse events were derived from an HEDM/IMS study of Belgian costs. Health state utilities were taken from the literature and supplemented by expert opinion. The model took a third-party payer perspective over 10 and 20-year time horizons. Both costs and outcomes were discounted at 3%.

Results: ANA, TAM-EX and TAM-LET were all associated with QALY gains and increased costs relative to TAM alone. CU improved over time as QALY benefits accumulated and outweighed up-front costs. At 10 years, relative to TAM alone, the CU of ANA was €48,323, TAM-EX was €14,147 and TAM-LET was €330,942. By 20 years, the CU of ANA was €19,992, TAM-EX was €4982 and TAM-LET was €10,548. Incremental CU comparisons between TAM-EX, ANA and TAM-LET were quite sensitive to relative differences in the hazard ratios and will be presented in a two-way sensitivity analysis. CU results for node negative and positive subsets will also be presented.

Conclusion: The CU of all three aromatase inhibitor strategies was favourable compared to TAM alone. Incremental comparisons among the AI options were sensitive to changes in the hazard ratios, but appeared to favour TAM-EX.

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Poster

After 10 years of follow-up, preoperative chemotherapy is still safe in operable breast cancer: Clinical and translational results from the European Organisation for Research and Treatment of Cancer Trial 10902

J.G.H. Van Nes¹, J.A. Van der Hage², J. Bogaerts³, I. Delmotte⁴, M. De Vos⁵, P. Therasse⁶, J.P. Julien⁷, M. Tubiana-Hulin⁸, C.J.H. Van de Velde⁹. *On behalf of the EORTC Breast Cancer Group. ¹Leiden University Medical Centre, Department of Surgery, Leiden, the Netherlands; ²Leiden University Medical Centre, Department of Surgery, Leiden, the Netherlands; ³EORTC, Department of Statistics, Brussel, Belgium; ⁴EORTC, Brussel, Belgium; ⁵EORTC, Brussel, Belgium; ⁶EORTC, Brussel, Belgium; ⁷Centre Henri-Becquerel, Department of Surgery, Rouen, France; ⁸Centre Rene Huguenin, Department of Oncology, Saint-Cloud, France; ⁹Leiden University Medical Centre, Department of Surgery, Leiden, the Netherlands*

Introduction: The Preoperative Chemotherapy in Primary Operable Breast Cancer (POCOB) trial was designed to evaluate whether preoperative chemotherapy (CT) in patients with primary operable breast cancer (BC) results in better overall survival (OS) and relapse free survival (RFS) rates and whether preoperative CT allows more breast-conserving surgery (BCS) procedures than postoperative chemotherapy. Additionally, tumour tissue was collected for translational research.

Patients and Methods: Patients (n=698) with operable BC (T1c, T2, T3, T4b, N0-1) were enrolled between 1991 and 1999 and randomised between CT administered preoperatively versus postoperatively. CT consisted of four cycles of fluorouracil, epirubicin, and cyclophosphamide. The primary endpoint was OS, secondary endpoints being relapse-free survival (RFS) and locoregional recurrence (LRR).

Results: With a median follow-up (FU) of 117 months there was no statistically significant difference between OS (hazard ratio (HR): 1.09; 95% CI (0.83–1.42); p=0.54), RFS (HR: 1.12; 95% CI (0.90–1.39); p=0.29) or LRR (HR: 1.16; 95% CI (0.77–1.74); p=0.48). Moreover, there was no statistically significant difference in time to distant progression (HR: 1.17; 95% CI (0.92–1.50); p=0.19) and time to second primary tumour (HR: 0.86; 95% CI (0.52–1.41); p=0.54). In the preoperative group, 37% of the patients underwent BCS in stead of a mastectomy compared to 21% of the patients in the postoperative group. With a median FU of 7 years, the p53 status was significantly correlated with the pathological tumour response and the clinical response (resp p=0.01 and p=0.008). Clinical tumour response was also predicted by clinical tumour size, tumour grade, p53 status, PgR status and HER2 status. There was no correlation between the p53 expression and OS (HR: 1.72; p=0.15).

Conclusion: Preoperative chemotherapy does not change the OS, RFS or the LRR in patients with breast cancer. Moreover, after 10 years of FU, there was no statistically significant difference in time to distant progression or to second primary tumours. This implies that preoperative chemotherapy is a safe procedure for patients with early breast cancer, even after a FU period of 10 years. Furthermore, it increases the amount of BCS. This most recent up-date of the POCOB will be presented together with translational research results with a median FU of 10 years.

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Poster

NCIC CTG MA17: Updated analysis on disease free survival (DFS) according to estrogen receptor and progesterone receptor status of the primary tumor

P. Goss¹, J. Ingle², D. Tu³. *On behalf of the MA17 Collaborative Trialists. ¹Massachusetts General Hospital, Cancer Center, Boston, USA; ²Mayo Clinic, Cancer Center, Rochester, USA; ³NCIC Clinical Trials Group, Cancer Research Institute, Kingston, Canada*

Introduction: Identifying biomarkers to predict response to adjuvant aromatase inhibitor therapy is important. In the ATAC trial (anastrozole vs tamoxifen) benefit of anastrozole over tamoxifen appeared restricted to the ER+ PgR- patients and not in those with ER+ PgR+ tumors. In contrast in subgroup analysis of the BIG1-98 trial the magnitude of benefit of letrozole vs tamoxifen on DFS did not vary according to PgR status. A central review of tumor tissue is currently being performed in this trial. MA.17 randomized 5187 postmenopausal women disease free after 5 years of tamoxifen to 5 years of letrozole or placebo. After 30 months median follow-up (range 1.5–61.4 months), the hazard ratio (HR) for DFS in the overall population was 0.58 (0.45–0.76, p=0.00004) in favor of letrozole. Almost all patients (97.4%) had estrogen receptor (ER) and/or progesterone receptor (PgR) positive primary tumors. We will present at the meeting the outcome of women according to the receptor status of their primary tumors, both in the intent to treat population of MA.17 (Letrozole and placebo patients) as