tamoxifen (TAM) and are associated with reduced survival. Reducing circulating estrogen levels may inhibit the growth of micrometastatic disease.
Methods: ATAC and BIG 1−98 are two trials evaluating the efficacy of adjuvant aromatase inhibitors (AIs) vs TAM in PMW with HD BC. BIG 1−98 is the only randomized phase III study comparing 5 years monotherapy with either TAM or letrozole (LET), and the sequential administration of both agents in either order. Efficacy results from the BIG 1−98 primary core analysis (PCA) at 26 months follow-up (FU) and monotherapy arms analysis (51M) at 51 months FU are presented. The PCA includes events in the monotherapy arms and in the sequential-treatment arms until 30 days post treatment switch (n = 8010). The 51M compares the 2 monotherapy arms (LET vs TAM for 5 years) (n = 4922).
Results: Compared with TAM, LET significantly reduced DM risk by 27% (P = 0.0012) in the PCA and by 19% (P = 0.03) in the 51M analysis. Populations from the PCA and 51M differ, and the impact of LET is greater in the PCA on the subgroup of patients with high risk of early recurrence (EaR). The ATAC and BIG 1−98 trials show that DM account for about two thirds of recurrences. In ATAC, at 2.5 years median FU, there were 7% fewer DM with anastrozole (ANA) vs TAM, while in the BIG 1−98, a pronounced impact on the early risk of DM was already seen at 2 years in patients treated with LET.
Conclusions: Differences between PCA and 51M results may be due to the natural history of early vs late risk of DM in HD BC. ANA and LET prevent EaR more effectively than TAM, but only LET appears consistently effective at reducing DM events at both 2.5 and 5 years. This observed difference in indirect comparison with ANA may be due to the greater suppression of estradiol by LET over ANA in HD BC. The FACE trial, comparing LET vs ANA in the initial adjuvant setting, should provide definitive results regarding differences between these two AIs.

2090 POSTER

Impact of sentinel lymph node biopsy before mastectomy and immediate reconstruction in predicting post mastectomy adjuvant radiotherapy. Does it improve the choice of the reconstruction?

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Background: Adjuvant post-mastectomy radiotherapy (RT), which is often unpredicted, is known to negatively affect the cosmetic outcome of immediate breast reconstruction (IBR).
Aim: To investigate the role of sentinel lymph node biopsy (SLN) in predicting RT and improving the choice of IBR.
Patients and Methods: All patients who had mastectomy and IBR between January 2004 and January 2007 were reviewed retrospectively. Axillary staging (clearance, sampling or SLN) was performed at the same time until October 2005 (Group1), when the unit's protocol was changed to perform SLN initially prior to mastectomy and reconstruction (Group2). Patients with positive SLN offered only a temporary sub pectoral tissue expander, while all options were offered if SLN was negative.
Results: 131 patients were reviewed (139 IBR). 20 patients had no axillary staging (DCIS, prophylactic mastectomy and phylloids tumour). 20 patients received unexpected RT in group1 (14 tissue expander, 4 LD with implant and 2 Free flaps) compared to 11 patients in group 2 who had a temporary tissue expander due to expected RT (P = 0.044).

	Group1 (67 IBR)	Group2 (72 IBR)
Axillary staging		
Clearance	47	19
Sampling	1	2
SLN	5[a]	45[b]
None	14	6
Reconstruction type		
Tissue Expander	33	35
LD/implant	16	6
LD	1	4
Free Flap	17	27

[a]2 patients had SLN biopsy and clearance. [b]7 patients had SLN biopsy and clearance.

Conclusion: SLN biopsy before IBR helps to predict RT and avoids its negative cosmetic effect on breast reconstruction. Patients with positive SLN biopsy are best offered a temporary sub pectoral tissue expander for IBR.

2091 POSTER

Biological effect of intraoperative boost with 50 kV X-rays in combination with external beam radiotherapy in early breast cancer

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Background: Intraoperative radiotherapy (IORT) with 50 kV X rays from a miniature X-ray machine (INTRABEAM®) is given as a boost to the tumour bed in one arm of the randomised TARGIT trial. Early clinical data showed a low incidence of fibrosis for the IORT boost combined with external beam radiotherapy (EBRT). The purpose of the present work was to model the risk of normal-tissue reaction and tumour recurrence as a basis for interpreting the clinical data.
Materials and Methods: Spherical applicators are used for tumour-bed irradiation with Intrabeam. The relative biological effectiveness (RBE) of 50 kV X rays was modelled based on the radial dose distribution using the linear-quadratic (L-Q) formalism including repair (Herskind et al. Radiat. Res. 163: 208−15, 2005). The dose of reference radiation was calculated from the physical dose distribution and the RBE and then converted to the equivalent dose of fractionated irradiation. The spatial distribution of risk of subcutaneous fibrosis and risk of recurrence were estimated from published clinical dose-response data.
Results: Fibrosis after irradiation with 50 kV X ray to the tumour bed alone is predicted to be confined to 3−4 millimeter depth of the tissue. The actual depth is likely to be smaller owing to the volume effect. However, when combined with 23x2 Gy EBRT to the whole breast, modelling calculations predicted a nearly 100% risk of fibrosis up to 10 mm depth or greater. The increased risk is related to the steep dose-response relationship for normal-tissue reaction. Clinically, however, moderate fibrosis of the tumour bed at 18 months follow-up was observed in only 8/70 (11%) of patients receiving IORT as a boost combined with EBRT. To study individual genetic factors influencing radiation-induced fibrosis, fibroblast cultures from unirradiated skin are being established within the GENEPI project. To date more than 50 patients from the IORT+EBRT group have been included. Modelling the risk of recurrence showed an advantage of combined treatment compared with conventional 25x2 Gy EBRT at up to 25 mm depth of the tumour bed.
Conclusions: The predicted risk of recurrence is consistent with the low recurrence rates observed clinically at early follow-up. By contrast, the observed rate of clinical fibrosis at 18 months was much lower (9-fold) than predictions. Although the rate may increase with longer observation time, we speculate that biological processes associated with surgery may render the late effects of the IORT boost and postsurgical EBRT subadditive.

2092 POSTER

Comparison of cost-effectiveness of aromatase inhibitors letrozole, anastrozole or exemestane versus tamoxifen for early breast cancer in hormone receptor-positive postmenopausal women: Canadian perspective

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Background: In postmenopausal women with early breast cancer, five years of letrozole (LET) or anastrozole (ANA), or sequential treatment with exemestane (EXE) following 2−3 years tamoxifen, is clinically superior to five years tamoxifen (TAM). Previous studies have assessed the economic impact of LET, ANA or EXE vs. TAM, separately. This analysis compares the cost-effectiveness of the aromatase inhibitors vs tamoxifen using the same health economic model from the Canadian perspective.
Methods: A Markov model was used to estimate the incremental cost per quality-adjusted life year (QALY) gained with initial adjuvant therapy with LET, ANA and EXE vs TAM. Probabilities of disease progression and adverse events were estimated using data from the BIG 1−98, ATAC and IES studies. Costs of breast cancer care and treatment of side effects, and health-state utilities were obtained from published studies. Costs and QALYs were estimated over the lifetime of a cohort of HR+ postmenopausal women with early breast cancer, aged 61 years at initiation of adjuvant therapy, and discounted at 5% annually.
Results: The incremental cost per QALY gained is $Can23,684 for letrozole vs tamoxifen, $Can29,433 for anastrozole vs tamoxifen and $Can28,932 for Exemestane vs tamoxifen. The deterministic sensitivity analyses suggest that the model results are most sensitive to the observed hazard ratios for breast cancer events. A larger impact on the results was also noted for older patients, primarily due to the higher general mortality rate that reduces the scope for benefit from the prevention of breast cancer events. The cost-effectiveness acceptability curve derived from the reference case analysis indicates that there is a 99% probability that the true incremental