Proffered Papers

(Neo)adjuvant medical treatment of early breast cancer

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Are international guidelines on adjuvant treatment for early breast cancer followed in clinical practice? A multicenter observational study on 1547 patients treated in 1997

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Purpose: To evaluate the consistency of clinical patterns of care, in the prescription of Medical Adjuvant Treatment (MAT) for Early Breast Cancer (EBC), with widely accepted international guidelines (JNCI 87: 1441–1445, 1995).

Methods: Within the framework of a prospective, multicenter, observational study performed by the AIRO-L cooperative group, data collected by 12 Radiotherapy centers on 1547/1610 pts with stage I–II breast cancer and irradiated to the breast in 1997 after conservative surgery have been analyzed (63 pts with no axillary dissection are excluded from this analysis).

Results:

(1) N+, premenopausal group: MAT was chemotherapy (CT) in 96%, hormonal (HT) in 0%, none in 4% of ER– pts; MAT was CT in 92%, HT in 4%, none in 4% of ER+ pts.
(2) N+, postmenopausal group: MAT was CT in 85%, HT in 10%, none in 5% of ER– pts; MAT was CT in 56%, HT in 40%, none in 4% of ER+ pts.
(3) N–, ER– group (high risk): MAT was CT in 59%, HT in 7% and none in 34% of pts.
(4) N–, ER+ group: the use of CT ranged from 0% (low risk pts) to 51% (high-risk, pre-menopausal pts); the option of no MAT ranged from 21% (high-risk pts) to 70% (low-risk pts).

Conclusions: A composite picture emerged from this analysis, with both over- and under-prescription of medical adjuvant treatment in different subsets of EBC patients, as compared with a specific example of international guidelines.

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Early breast cancer: How long should tamoxifen continue?

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The overview by the Early Breast Cancer Trials Collaborative Group analysed data on ~37,000 women in 55 trials of adjuvant tamoxifen (TMX). For women with receptor positive disease, or with unknown receptor status, TMX is of substantial benefit, regardless of age or nodal status. 5 years of TMX appears better than 2 years. The effects of more than 5 years of TMX could not be assessed because there was insufficient randomised evidence to look at this reliably. Until trials that randomise 5 years versus longer hormonal therapy have entered and followed large numbers of women for many years, this question will remain unanswered. In particular, trials of this question that have already closed leave major uncertainty as to whether treatment should routinely continue beyond the fifth year.

ATLAS is an international trial of longer versus shorter hormonal therapy to assess reliably the effects of an extra 5 years of TMX in women who have had some years of treatment and for whom there is uncertainty as to whether they should now stop, or continue. 10–20,000 women will be randomised, usually after about 5 years of TMX, to either stop, or continue TMX for 5 more years. This large, simple trial addresses a question of relevance in routine clinical practice into which it is easily integrated. The main analysis will be of all-cause mortality, but ATLAS will also provide information on cause-specific mortality and non-fatal, but important, events. If, by 2010, ATLAS shows improved long-term survival with 10 years of TMX, this result will save thousands of lives annually, and will be relevant to the appropriate use of hormonal therapies in general. By September 1999, more than 5000 women will have entered ATLAS making it the largest ever study of tamoxifen duration. Still however, many thousands more need to be randomised to answer this question definitively. New collaborators are invited to join the study.

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Adjuvant CMF (cyclophosphamide, methotrexate, fluorouracil) in breast cancer. Is it cost-effective?

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Introduction: Today, adjuvant chemotherapy (ACT) consisting of CMF is standard practice in several countries. Benefits in delayed time to recurrence and prolonged survival has been documented. The incidence of breast cancer suggests a significant financial burden to the health care system.

Material and Methods: The cost-effectiveness analysis included data from the English speaking literature on efficacy, tolerability and quality of life (QoL) and Norwegian data on age, survival, drug charges and production gains/losses. The median age of women undergoing ACT in Norway was 50 years, the CMF regimen saved 0.51 years per woman treated during 10 years (Milan study), a survival gain of 8.5% after 10 years and a life expectancy of women aged 60 of 22.8 years. The efficacy was then measured 2.45 years saved per patient treated. The QoL was assumed diminished by 0.33 (0–1 scale) for 6 months during ACT, the life years (LY) gained valued Q = 0.86 and the dose intensity 85%. It was calculated 1 BP (£) = 12NOK and a 5% discount rate.

Results: The total cost of adjuvant CMF was calculated £1,976. Money spent on drugs alone constituted 41%. The cost per LY saved was measured £1,784. A sensitivity analysis was done. An off by 10% on drug charges indicated a cost per LY gained of £1,280. If the women were not cured by CMF, but lived half of their expected life span, the figure was £1,830. If 2% of ACT patients had been hospitalised due to sepsis, the total cost per patient had raised by £89.

Conclusion: Adjuvant CMF in breast cancer is cost effective in Norway.

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Neoadjuvant chemotherapy for breast cancer (BC): Is doxorubicin-cyclophosphamide (AC) combination still a standard regimen?

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Purpose: The NSABP B18 trial established AC as a standard neoadjuvant regimen for BC. In a randomized phase II trial, AC was evaluated Vs doxorubicin – TAXOL® (AT). Primary objective: pathological complete response (pCR); secondary: clinical response and safety.

Methods: Prospective, unbalanced randomized (2AT:1AC), parallel, multicenter trial. Pts were stratified according to center and tumor size (T2, T3). Treatment consisted of 4 cycles of AT: doxorubicin 60 mg/m^2 and TAXOL® 200 mg/m^2 as a 3-hour-infusion, or AC: doxorubicin 60 mg/m^2 and cyclophosphamide 600 mg/m^2, followed by surgery, radiotherapy and tamoxifen for postmenopausal ER+ pts.

Results: A planned interim analysis (AC: 40 pts – AT: 80 pts) was performed according to early stopping rule of less than 7.5% of pCR: AC arm was stopped (5% pCR). Accrual continued in AT arm up to 180 pts. As