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Assessment of an algorithm for prevention of aromatase inhibitor-associated bone loss: two year results

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Background: Aromatase inhibitors (AI) are increasingly becoming the adjuvant endocrine therapy of choice in postmenopausal women with endocrine-responsive early breast cancer. AIs are associated with decreased bone mineral density (BMD) and a subsequent increase in fracture risk, so patients should be monitored for AI-associated bone loss (AIBL) with intervention introduced where appropriate.

Methods: The BATMAN trial (ClinicalTrials.gov ID NCT00122356) is based on an algorithm proposed by Osteoporosis Australia in 2005, where intervention with bisphosphonates is dependent on changes in BMD and N-telopeptide (NTx), a bone resorption marker. An interim analysis of 143 early breast cancer patients with at least 1 year follow-up has been performed to assess the impact of an AI on patients with normal BMD, osteopaenia or osteoporosis at baseline. All patients received anastrozole (1 mg), calcium ($\geqslant$500 mg) and Vitamin D ($\geqslant$400 IU) supplements.

Results: At baseline, 8 (6%) of the 143 patients were classified as osteoporotic, 68 (47%) were osteopaenic and 67 (47%) had a normal BMD. Baseline Vitamin D levels were deficient ($\leqslant$50 nmol/L) in 38% of all patients. Osteoporotic patients received alendronate (70 mg once weekly) which resulted in decreased NTx after 6 months and increased BMD after 1 and 2 years of therapy. NTx increased in osteopaenic and normal BMD patients not receiving alendronate. After 1 year of anastrozole, the BMD of osteopaenic patients decreased by a mean of −1.4% (lumbar spine, LS) and −1.8% (neck of femur, NOF) from baseline. In accordance with the algorithm, 7 osteopaenic patients commenced alendronate at this time-point. After 2 years of anastrozole, the BMD of osteopaenic patients who had also received 1 year of alendronate increased by 3.0% (LS) and 3.6% (NOF) while osteopaenic patients only on anastrozole had a decreased BMD of −2.1% (LS) and −2.0% (NOF). Three of these patients commenced alendronate at 2 years as guided by the algorithm. Thus far no patients with a normal BMD at baseline have required alendronate intervention.

Conclusions: Patients are accumulating significant BMD losses over 2 years of anastrozole but the requirement for intervention with alendronate has been lower than expected, especially in patients with a normal baseline BMD. Patients who have triggered the algorithm are demonstrating a reversal in AIBL with bisphosphonates. Baseline assessment, monitoring, then intervention when required is appropriate in AIBL.

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Impact of breast cancer treatment on lymphedema and impairment of function − A nationwide study of prevalence and associated factors

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Background: Lymphedema and impairment of function are well-established sequelae to breast cancer treatment and affects an increasing number of women due to continually improved survival.

The aim of the present nationwide questionnaire study was to examine the impact of breast cancer treatment on swelling/sensation of heaviness of the arm (lymphedema) and on function, reporting prevalence in 12 subgroups of modern standardized treatment and offering estimates for treatment related associated factors.

Material and Methods: The study was based on a nationwide cross-sectional questionnaire study, also dealing with pain and sensory disturbances [1], performed spring 2008 of women operated for primary breast cancer in Denmark between 2005 and 2006 divided into 12 well-defined treatment groups. Adjusted odds ratios were calculated for reported lymphedema and impairment of function with respect to age, surgical technique, chemo- and radiotherapy.

Results: 3253 women returned the questionnaire (response rate 87%). 1249 (38%) reported swelling or sensations of heaviness of which 12% reported severe swellings/heaviness, 38% moderate, and 50% light.

The prevalence of reporting swellings/heaviness varied from 13% to 65% depending on treatment group. Associated Factors were young age, axillary lymph node dissection and adjuvant radiotherapy but not mastectomy or chemotherapy.

787 patients (24%) reported that they have had to give up activities after treatment for breast cancer, 22% reported that it had affected their work and 22% that it had affected their sports-activities. The prevalence of having to give up activities varied from 11−44% depending on treatment group. The most important predictors for impairment of function was pain and swellings/heaviness of the arm, but younger age, ALND, chemotherapy, short observation time since operation, and being operated on the dominate side were also associated with an increased risk of reporting impairment of function. Radiotherapy and type of surgery to the breast was of no importance.

Conclusions: 2−3 years after breast cancer surgery more than one third of the patients report swellings/heaviness of the arm and one in four reports functional impairment. The prevalence varied considerably between treatment groups.

References

[1] Gärtner R, Jensen MB, Nielsen J, Kvistgaard ME, Kroman N, Kehlet H. Prevalence of and factors associated with persistent pain following breast cancer surgery − A nationwide study. *JAMA* 2009; 302(18): 1985–1992.

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Genetic variation in relation to adverse side-effects of radiotherapy − focus on the metabolism of reactive oxygen species

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Background: Improved detection and early diagnosis of cancer are likely to increase the importance of loco-regional control and hence the significance of radiotherapy (RT). Like most therapies, RT has the power to heal but also to harm and are associated with a wide-range of long-term complications depending on the properties of the administered therapy and the tissue affected by the malignancy. In this study we investigate the influence of genetic variation in genes metabolising reactive oxygen species on the level of radiation induced adverse side effects in breast cancer (bc) patients and the expression level in fibroblasts. The aim is to identify genetic markers of normal tissue radiosensitivity and examine the possible link between associated expression profiles and the genetic background.

Materials: 92 Norwegian bc patients treated with hypofractionated RT (4.3 Gray $\times$10) were analysed for adverse effect of treatment for the following end-points: athrophy, subcutaneous (sc) fibrosis, costal fractures, telangiectasias and pleural thickening. In addition, the study includes the analysis of both unirradiated and irradiated fibroblast cell lines analysed with whole genome expression profiling. The cell lines were established from samples collected from 33 Danish bc patients evaluated for the development of subcutaneous fibrosis following RT.

Results: For all clinical end-points studied, we identified SNPs significantly associated with the level of adverse by two different statistical methods (Mutual information score (MIS) and Chi-square/the Cochrane Armitage trend test): The identified SNPs are for costal fractures (4 SNPs, rs670548 in GCLC, rs743409 in MAPK1, rs314156 in KCNMB1 and rs2159132 in COX10), pleural thickening (3 SNPs, rs1143623 in IL1B, rs314674 in PRKD2 and rs2037547 in NR1I2), telangiectasias (1 SNP, rs511895 in CAT), atrophy (3 SNPs, rs2229765 in IGF1R and rs1126647 and rs4073 in IL8) and subcutaneous fibrosis (7 SNPs, rs744751 and rs731465 in TGFBR2, rs1139793 in TXNRD2, rs945222 in MGMT, rs1934951 in CYP2C8 and rs2227306 and rs4073 in IL8).

With regards to the fibroblast cell lines, expression studies have previously identified a list of 18 genes (*e.g. MTF1*, *CCND2* and *LUM*) predictive of the risk of developing radiation induced sc fibrosis after treatment. Our results indicate that the expression level of several of these genes is influenced by the genetic background in genes such as *EGF*, *EGFR*, *EPHX2*, *PDGFRA* and *TGFB2. EPHX2* was also found associated to the level of sc fibrosis in the Norwegian samples (only significant by one of the methods (MIS)).

Conclusion: Genotype profiling of patients before therapy administration may help to identify those individuals who will not respond to a given treatment or who are likely to suffer potentially severe side effects.