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Optimal prevention of bone loss due to aromatase inhibitors in early non-metastatic breast cancer after menopause

Background: Breast cancer (BC) is the most common cancer in women. In postmenopausal women with estrogen receptor (ER) dependent BC, anti-hormone therapy is an option with aromatase inhibition (AI), resulting in decreased estrogen production. Available therapeutic options for management of bone loss in patients receiving AI are zoledronic acid (ZA), risedronate (Ris), alendronate (Aln) and denosumab (Dmab). Current knowledge on anti-neoplastic effects favors ZA. However in cases of more severe disease Dmab might be superior.

Methods: In PubMed and Embase, 373 studies were identified on Al treatment and BMD or fracture. In total, 31 RCT studies was found during the evaluation; ZA 18, Ris 9, Aln 2 and Dmab 2.

Results: Evaluation of ZA treatment showed 18 RCT studies on BMD or fracture. However in several cases the cohorts were reported on more than once. We found in total 7 cohorts evaluated after 12 to 61 months. In all cohorts the treatment was ZA acid 8 mg/year vs. placebo (n= 1,551 vs. 1,550). The absolute difference in mean lumbar spine and total hip BMD's between patients in treatment or placebo was 8.9% and 5.9%, respectively. None of the studies reported severe side effects. The evaluation of Ris treatment showed 8 RCT studies on BMD or fracture. However, 1 study was reported only on bone markers. Of the remaining 7 studies, 2 studies were excluded. The 2 studies excluded were 1 study on a mix of Aln and Ris and 1 study of 6 month length and 2.5 mg Ris per day. The remaining 5 studies reported were 24 month RCT's. In all 5 studies the treatment was Ri 35 mg/week vs. placebo (n= 429 vs. 291). The absolute difference in mean lumbar spine and total hip BMD's between patients in treatment or placebo was 4.5% and 3.1%, respectively. Two RCT's are published on Aln of whom only one study had a long time follow-up (36 months). None of the studies on bisphosphonate reported severe side-effects. Evaluation of Dmab treatment showed 9 RCT papers where two papers reported on BMD and fracture. These papers were on the same cohort and they reported on 24 mo of Dmab 60 mg every 6 mo vs. placebo (n= 123 vs. 122) an absolute mean lumbar difference in spine BMD of 7.6% and no severe side-effects.

Conclusion: Among anti-resorptives, ZA currently has the highest evidence for prevention of Al associated bone loss in postmenopausal women with early BC. Data on fracture prevention is sparse.

Biography

Peter Schwarz is a Professor at the Department of Endocrinology, Rigshospitalet, Denmark and is covering a broad clinical and laboratory experience from employment in departments of Internal Medicine and Clinical Biochemistry focusing calcium metabolic diseases and secondary osteoporosis at Copenhagen University. Clinically, he is a Chief Physician covering especially secondary bone loss and secondary osteoporosis due to treatment of breast cancer treatment. Breast cancer is the most common cancer in Danish women, and has an average of about 5.000 new cases a year. Patients treated for early (non-metastatic) breast cancer comprise, due to earlier diagnosis and improved treatment, a large and growing group of cancer survivors. However, many patients experience treatment-related endocrine side-effects such as reduced bone mineral density, dyslipidemia, insulin resistance and hypertension increasing the risk of bone fractures as well risk of development of metabolic disease. The research group is focused to understand the underlying physiological and molecular mechanisms responsible for the chemotherapy-induced bone and cardiometabolic derangements to identify novel disease mechanisms as well as to identify potential biomarkers to be used for better prediction and prevention of metabolic disease. Targeted exercise training could reduce treatment-related risk of metabolic disease and of bone fractures and the research group aims to investigate the effect of physical activity on minimizing or reversing treatment-related side-effects. He has published 138 original papers, editorials and reviews and authored 6 book chapters.

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