SAT0152 EFFECTS OF RALOXIFENE ON BONE MINERAL DENSITY AND ON SERUM LIPIDS IN POSTMENOPAUSAL WOMEN WITH SEVERE OSTEOPENIA AND/OR OSTEOPOROSIS

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Background Raloxifene (RLX) is a selective oestrogen receptor modulator (SERM) and exerts a positive estrogenic activity on bone and on serum lipids. The purpose of this randomised study was to access the effect of RLX on Bone Mineral Density (BMD) and on serum lipids in postmenopausal (PM) women with severe osteopenia and/or osteoporosis according to WHO criteria.

Objectives 100 PM women were randomly assigned to either RLX 60 mg/day+600 mg Calcium Carbonate (CC) (70 women) or 600 mg of CC alone (30 women), as controls, for 12 months. The two groups of women had similar anthropometric data, mean age ($56,98 \pm 5,1$ yrs) and mean postmenopausal age ($9,4 \pm 5,2$ yrs).

Methods BMD was measured at baseline and at 12 months of therapy, using DEXA (Hologic 1000 QDR) at Lumbar Spine (LS) and Lft Femur (FN)(neck). Serum total Cholesterol, LDL, HDL, triglycerides were measured at baseline, 6 and 12 months (photometric method). Results are expressed as percentage change from baseline. Statistics were done using t-test (unpaired).

Results Bone loss prevented only in the group of RLX. The BMD increased at LS = $+2,3(\pm 2,8)\%$ and at FN = $1,4 (\pm 2,6)\%$. In the group of controls the BMD diminished at LS $-1,2 (\pm 1,1)\%$ and at FN $-1,5(\pm 2,4)\%$. The difference in BMD changes between the two groups was significant ($p < 0,05$). There was no change in HDL, LDL and triglycerides in either group. Only Total Cholesterol decreased significantly ($p < 0,05$) in RLX group. No clinically relevant effects on safety parameters (liver enzymes, hematologic variables and vital signs) were recorded.

Conclusion We conclude that RLX proved to be effective and safe in the prophylaxis and treatment of postmenopausal severe osteopenia and/or osteoporosis.

SAT0153 VERTEBRAL DEFORMITIES IN RHEUMATOID ARTHRITIS: THE OSLO, TRURO, AND AMSTERDAM COLLABORATIVE STUDY

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Background

Objectives To determine the occurrence of vertebral deformities (VD) in a cross-sectional study of postmenopausal women with rheumatoid arthritis (RA). Secondly, associates for VD will be identified.

Methods A total of 150 female patients (50 per centre), aged between 50 and 70 years and a disease duration of 5 or more years, attending a general rheumatology clinic were consecutively included. Demographic and clinical data were collected according to a standardised procedure; bone fracture history, disease activity measures, hand X-rays (Larsen) and bone mineral density by means of dual energy X-ray absorptiometry of hip and

lumbar spine. Lateral X-rays of thoracic and lumbar spine were read by one observer. Assessment was done as proposed by Genant.¹ Associations between the presence of VD, and demographic, clinical and BMD variables were examined bivariately. The multivariate analysis was carried out using logistic regression.

Results Spine X-rays of 137 women were included in the analysis. Of these women 20 out of 137 (14.6%) had at least one VD grade one or higher; 18% in Oslo, 10% in Amsterdam, and 16% in Truro. The table shows results of the bivariate analysis. Ever use of corticosteroids was not associated with VD ($p = 0.33$).

Previous non-vertebral fracture after age 25 (as recalled by the patient) was the independent associate for VD in a logistic regression model containing age, weight, total Larsen score, non-vertebral fracture after age 25 and either femoral neck or spine BMD. Femoral neck BMD was independent variable in a model with age, weight, total Larsen score and femoral neck BMD. Age was the only independent associate of VD if femoral neck BMD was replaced by spine BMD in the latter model. The inclusion of corticosteroid use in either one of the models did not change the results.

Abstract SAT0153 Table 1

	Age (years)	Non-vertebral fracture (%)	Total Larsen score (0-120)	Femoral neck BMD (g/cm ²)	Spine BMD (g/cm ²)
no VD	60.7	21.6	37.9	0.81	1.07
VD	64.4	55.0	53.4	0.70	0.98
p- value	0.009	0.02	0.03	0.006	0.05

Conclusion VD in a clinic population of RA patients was associated with either previous clinical fracture, femoral neck BMD or age as single independent variable dependent on the regression model applied. Studies on more patients allowing for larger regression models should further clarify the true associates of VD.

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SAT0154 BISPHOSPHONATES AND UPPER GI PROBLEMS – WHAT IS THE EVIDENCE?

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Background Upper gastrointestinal (UGI) tract mucosal irritation has been reported for a variety of bisphosphonates, including pamidronate, etidronate, clodronate, alendronate (ALN), tiludronate, and risedronate (RIS).

Objectives To use evidence-based medicine to rate and summarise the evidence regarding bisphosphonates and UGI problems.

Methods Review and interpretation of published studies.

Results Although the clinical relevance of short-term, transient endoscopic findings is uncertain, one endoscopic study reported a higher incidence of gastric lesions for ALN vs RIS, and others reported no difference for ALN vs RIS or placebo.¹⁻⁴ These

endoscopic studies differed in regard to blinding, duration, and control. Endoscopy trials that were appropriately blinded and of longer duration (4–10 wks) found no difference between ALN and RIS or placebo, even at the higher doses used for once-weekly dosing⁴ or to treat Paget's disease.³ Randomised, blinded, controlled trials (RCTs) with clinically relevant GI endpoints represent the highest level of evidence, and tens of thousands of patients have participated in RCTs of ALN and RIS for up to 7 years. UGI complaints were common in these studies (~30% in the first year), and were comparable to placebo. In particular, the incidence of more worrisome UGI events (including esophageal events, and gastroduodenal perforations, ulcers, and bleeds) was low and comparable to the placebo group, even in high risk subgroups, among 6459 women randomised to ALN or placebo for up to 4.5 years in the Fracture Intervention Trial.⁵ Furthermore, two independent RCTs of patients who had previously reported intolerance to bisphosphonate reported that the large majority (~85%) were able to continue ALN or RIS when treatment was resumed, and the permanent discontinuation rates were no different from the placebo group.^{6,7}

Conclusion Based on extensive data from large RCTs, we conclude that any increase above placebo in clinically relevant UGI problems related to bisphosphonate use is very low – too low to detect in trials involving thousands of participants during several years of follow-up.

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SAT0155 PREVALENT VERTEBRAL FRACTURES ARE ASSOCIATED WITH PHYSICAL IMPAIRMENT

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Background Vertebral fractures are a hallmark of postmenopausal osteoporosis and an important end point in trials of osteoporosis treatment, but the clinical significance of prevalent fractures remains uncertain.

Objectives To examine the associations of prevalent vertebral fractures and other characteristics with physical functioning among 589 Japanese women ages 40 to 90 years.

Methods Lateral spine radiographs were obtained and radiographic vertebral fractures were assessed by quantitative morphometry, defined as vertebral heights more than 3 SD below the normal mean. A self-administered questionnaire was used to survey participants about difficulty in performing selected basic and instrumental activities of daily living (ADL).

Results The prevalence of vertebral fractures increased significantly with age. Half of women ages 80 and over had vertebral fractures. Impaired function was defined as difficulty performing 3 or more ADLs. Each vertebral fracture increased the odds of impaired function by 1.4 times (95% CI: 1.1, 1.8) in an age-adjusted logistic regression model. The number of vertebral

fractures remained a significant predictor independent of age, number of painful joints, and BMI in multiple variable logistic regression models; the odds ratio of impairment for number of vertebral fractures was 1.5 (CI: 1.2, 2.0). Additional adjustment for back pain did not alter these findings.

Conclusion The number of prevalent vertebral fractures contributed significantly to impaired function. The association was independent of age, back pain and the number of painful joints. The results also suggest that vertebral fractures may impair physical function even when back pain is not present.

SAT0156 PREDICTORS OF BONE MINERAL DENSITY IN HEALTHY MALES

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Background Osteoporosis (OP) is a growing health problem not only in women but also in men. It is well known that men lose bone during ageing and are at risk for OP, but the risk factors for OP in men remains controversial.

Objectives The aim of this study was to assess determinants of bone mineral density (BMD) at the lumbar spine and femoral neck in healthy males.

Methods Thirty-seven healthy men aged 43–73 years were included in this study. BMD was measured using dual photon absorptiometry. Predictors of lumbar spine and femoral neck BMD were determined using multiple linear regression analysis. Backward elimination procedure was used to identify variables significantly related to BMD. The independent variables entered the regression model included age, body mass index (BMI), smoking history, alcohol intake, urinary calcium and hydroxyproline, and serum concentrations of osteocalcin, parathyroid hormone, testosterone, growth hormone, and cortisol.

Results The mean age of the men was 59.8 ± 6.8 years. Mean BMD at the lumbar spine was 0.97 ± 0.10 gr/cm² and that of the femoral neck was 0.76 ± 0.06 gr/cm². Backward elimination procedure was used to identify variables significantly related to BMD. The independent variables entered the regression model included age, body mass index (BMI), smoking history, alcohol intake, urinary calcium and hydroxyproline, and serum concentrations of osteocalcin, parathyroid hormone, testosterone, growth hormone, and cortisol. Backward regression analysis indicated that testosterone, cortisol and BMI were significant predictors of BMD at the lumbar spine ($R = 0.44$, $p < 0.05$) while testosterone, hydroxyproline and osteocalcin were significant predictors of BMD at the femoral neck ($R = 0.20$, $p < 0.05$). Testosterone, cortisol and BMI accounted for 44% of the total variance in lumbar spine BMD, and testosterone, hydroxyproline and osteocalcin accounted for 20% of the total variance in femoral neck BMD. Men with lower BMI had significantly lower bone mass at the lumbar spine ($r = 0.43$, $p < 0.05$). In addition, men with lower bone mass at the lumbar spine had significantly higher serum cortisol levels ($r = -0.33$, $p < 0.05$).

Conclusion These observations suggest that testosterone, cortisol and BMI are main determinants of lumbar spine BMD, while testosterone, urinary hydroxyproline and osteocalcin are main determinants of femoral BMD in our group of healthy men.