OC1
AN INVERSE ASSOCIATION BETWEEN SERUM UNDERCARBOXYLATED OSTEOCALCIN LEVELS AND BLOOD GLUCOSE AND HEMOGLOBIN A1C LEVELS IN AN ELDERLY JAPANESE MALE POPULATION: FUJIWARA-KYO OSTEOPOROSIS RISK IN MEN (FORMEN) STUDY
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Aims: Several animal-based studies reported that undercarboxylated osteocalcin (ucOC) enhanced insulin sensitivity and improved glucose tolerance(1–3), while such hormonal functions were reported in association with carboxylated OC in Caucasian people(4). We aimed to clarify whether serum ucOC levels are associated with glycemic status in a population of elderly Japanese men.

Methods: We analyzed the data from the FORMEN Baseline Study, an ancillary study of a larger cohort study, the Fujiwara-kyo Study(5). We included 2,174 male participants of the Fujiwara-kyo study (≥65 years) who were able to walk without aid from others and lived at home in four cities of Nara Prefecture. We excluded participants with a history of diseases or medications that affect bone metabolism, other than type 2 diabetes mellitus (T2DM). Main outcome measures were fasting plasma glucose (FPG) and glycated hemoglobin A1c (A1c) levels which were examined for an association with serum ucOC as well as intact OC (iOC) levels after adjusted for potential confounders. Mean values of FPG and A1c showed a significant decreasing trend with higher quintiles of iOC or ucOC after adjusting for confounders. This trend remained significant for ucOC quintiles after further adjustment for iOC levels, but was not significant for iOC quintiles after adjusting for ucOC levels (Figure). These results were attenuated, but remained significant after excluding participants receiving drug therapy for T2DM.

Results: Of the 1,597 participants included in the analysis, both iOC and ucOC levels showed significant inverse correlations with FPG and A1c even after adjusting for

Conclusions: Levels of ucOC, but not iOC, hence, not carboxylated OC, were associated inversely with FPG and A1c in a population of Japanese men. Thus, ucOC may play an important role in glucose metabolism in humans.

References: (1) Lee NK, et al. Cell 2007;130:456
Aims: The femoral neck is likely to fail through two mechanisms: local elastic buckling, or yielding. [1] Local elastic buckling occurs when a portion of the cortex abruptly bulges inwards or outwards. Yielding occurs when bone material disintegrates at a microscopic level, initiating a crack that develops into a full fracture. We hypothesized that local elastic buckling is prevented by dense trabecular networks that provide lateral support to the cortical shell, implying that elderly people suffer a greater risk of fracture by buckling.

Methods: 3D models of the femoral neck were generated using Mimics software (Materialise Inc, Ann Arbor, MI, USA) from the intact femora of eight human cadavers. The narrowest cross-section of the femoral neck was chosen for buckling analysis. Material properties of cortical elements were computed from the mean CT numbers associated with each element. The Finite Strip Method was then implemented using the CUFSM software (www.ce.jhu.edu/bshafer/cufsm/) on the two models: cortex only, and cortex with trabeculae. Winter’s equations were applied on the buckling load values to establish whether the bone ultimately failed by elastic buckling or yielding. Bone remodelling with age was simulated for young, middle-aged, and the elderly, and similar analysis performed. The contribution of the trabeculae to the total bone strength was determined for all the models.

Results: The local buckling shapes for models at various ages and different load adaptations were considerably different. The local buckling strength of cortical shells decreased with an increase in age for all subjects. The trabecular core contributed between 18% and 49% to the strength of the femoral neck. The buckling strength contribution of the trabecular core was found to decrease with an increase in age for all subjects.

Conclusions: Local buckling strength depends considerably on the mean thickness of the thinnest segment of the cortical shell, which is usually located between the superior and posterior regions of the section. Hence, local buckling was found to be initiated between superior and posterior regions. Just prior to the onset of buckling, the trabecular core reinforces the cortical shell by providing lateral support. The trabecular core is not mechanically capable of providing sufficient strength against yielding. Age-related bone remodeling results in thinning of the cortices and loss of trabecular bone, which contribute to the observed decrease in the pure elastic buckling load and predicted strength. Contribution of the trabecular core to the overall strength did not vary considerably with respect to percentage of habitual load adaptation, due to the negligible structural changes that occurred in the remodeling of trabecular core.


Acknowledgements: The Fujiwara-kyo Study Group (chaired by Norio Kurumatani with Nozomi Okamoto as secretary general) comprising Nobuko Amano, Yuki Fujita, Ak hi ro Harano, Kan Hazaki, Masayuki Iki, Junko Iwamoto, Akira Minematsu, Masayuki Morikawa, Keigo Saeki, Noriyuki Tanaka, Kimiko Tomioka and Motokazu Yanagi, performed most non-skeletal measures in the present study and provided the data to the FORMEN Study.

Disclosure of Interest: M. Iki Grant/Research Support from: the Japan Dairy Association, Consultant/Speaker’s bureau/Advisory activities with: the Japan Dairy Association, J. Tamaki: None Declared, Y. Fujita: None Declared, K. Kouda: None Declared, A. Yura: None Declared, E. Yanagi, performed most non-skeletal measures in the study.

fractures. As one of the possible applications of FRAX®, the Japanese committee on FRAX® examined the way to use FRAX® as a measure for treatment threshold of osteoporosis. The core policy of our way in seeking the threshold was that the proposal should conform with and support the current clinical guideline in Japan.

**Methods:** The current Japanese guideline for the prevention and treatment of osteoporosis recommends pharmacological therapy for the patients with fragile osteoporotic fractures, those with bone mineral density (BMD) lower than 70% of young adult mean (YAM), and those of osteopenia with one of the clinical risk factors (smoking, excessive alcohol, parents’ history of hip fracture). We calculated the FRAX® risk in the patients under the pharmacological treatment of osteoporosis according to this guideline at independent clinics. Because the incidence of vertebral fractures in Japanese is much higher than that in Caucasians, we focused on the 10-year risk for major osteoporotic fractures as the FRAX® risk in this study. Then, proportion of those who will have the 10-year risk over some cut-off values were examined for general population and hospital samples. The observed incidence of vertebral fractures in the prospective cohorts was compared with the FRAX® risk. Taking these results together, a treatment threshold was proposed for Japanese.

**Results:** The mean FRAX® risk of the patients under treatment according to the Japanese guideline distributed around 15–20%. When the effects of three tentative cut-off values (10, 15, 20% for major osteoporotic fractures) were examined in general populations, 15% seemed reasonable for the proposal. However, more than 90% of women aged 75 or older had the risk higher than this cut-off value. In addition, substantial percentage of younger women with normal BMD had the FRAX® risk higher 15%. These results indicated that age and/or BMD should be considered when a single threshold of FRAX® is applied for Japanese. The incidence of vertebral fractures in the prospective cohorts was higher than that predicted by FRAX®, showing one of the limitations of FRAX® in clinical application.

**Conclusions:** The committee recommends the cut-off value of 15% for major osteoporotic fractures in the patients with osteopenia (YAM 70~80%), but this cut-off value is applicable for the women under 75-year old. FRAX® will give a track of clinical decision which is additional to the current Japanese guideline. Younger patients, e.g., those in fifty, should be assessed by the current guideline. The limitations of FRAX® in clinical application should be considered further.

**Disclosure of Interest:** None Declared

**Aims:** Postmenopausal osteoporosis is a chronic disease requiring long-term treatment. Strontium ranelate (SrRan) 2 g/day has proven efficacy against vertebral and non vertebral fractures including hip over 5 years in postmenopausal women. Results showing the continuous benefit on osteoporotic fractures and bone mineral density (BMD) over 8 years have already been reported (1). This abstract presents efficacy results over 10 years.

**Methods:** The two double blind placebo-controlled phase III studies included a total of 6,740 Caucasian women with postmenopausal osteoporosis. In SOTI, patients were randomly assigned to receive SrRan 2 g/day or placebo for 4 years and during the 5th year, half of the SrRan group continued with SrRan. In TROPOS, patients were randomly assigned to receive SrRan 2 g/day or placebo for 5 years. Patients having participated in both studies up to 5 years were invited to enter a 3-year open-label extension study, subsequently extended by 2 years, and then received strontium ranelate up to 10 years. Here are presented the efficacy results in patients treated with SrRan for 10 years.

**Results:** At SOTI and TROPOS baseline, patients treated for 10 years (n=233) had a profile similar to the whole population with a mean (SD) age of 72.0(5.5) years, a mean (SD) lumbar spine and femoral neck BMD T-score of −2.95(0.57), respectively. Over the 10-year period, lumbar BMD increased continuously and significantly (p<0.05 up to year 10) with, at 10 years, a relative change from baseline of 34.5%±20.2. At the femoral neck and total hip sites, the BMD increased significantly until year 7, with a relative change from baseline of 10.7%±12.1 and 11.7%±13.6 respectively, and then remained stable. To assess the anti-fracture efficacy of SrRan in the absence of placebo group, the incidences of fracture in the population treated for 10 years over the 5 years of SOTI/TROPOS and the 5 years of their extension were compared. The cumulative incidences of new vertebral and non vertebral fractures (20.6% and 13.7%, respectively) over the 5-year extension were not statistically
different \( (p=1.00 \text{ and } 0.672, \text{ respectively}) \) to the cumulative incidences over the 5 years in the original studies (18.5\% and 12.9\%, respectively) despite a theoretical increase of fracture risk with ageing. Strontium ranelate remained safe and well tolerated over 10 years with no unexpected adverse event.

**Conclusions:** The incidence of vertebral and peripheral fractures over the 5-year follow-up was comparable to the incidence observed in SOTI and TROPOS at 5 years, in spite of a fracture risk theoretically increased by age. These results are in favour of the maintenance of the efficacy of strontium ranelate over 10 years, with a good safety profile.


**Disclosure of Interest:** J. Y. Reginster Grant/Research Support from: BMS, MSD, Rottapharm, Teva, Lilly, Novartis, Roche, GSK, Amgen and Servier, Consultant/Speaker’s bureau/Advisory activities with: Negma, Wyeth, Amgen, UCB, MSD, Lilly, Rottapharm, IBSA, Genevriër, Novartis, Servier, Roche, GSK, Teijin, Teva, Ebewee Pharma, Zodiac, Analis, Theramex, Nycomed, and Novo-Nordisk, J.-M. Kaufman Grant/Research Support from: Amgen, Daiichi-Sankyo, GSK, MSD, Novartis, Nycomed, Servier and Roche’s bureau/Advisory activities with: Amgen, Daiichi-Sankyo, GSK, MSD, Novartis, Nycomed, Servier and Roche, S. Goemaere Consultant/Speaker’s bureau/Advisory activities with: Servier, C. L. Benhamou: None Declared, A. Balogh: None Declared, C. Albanese: None Declared, J. Badurski: None Declared, C. Roux Grant/Research Support from: Servier, MSD, Amgen, Novartis, Roche and Lilly, Consultant/Speaker’s bureau/Advisory activities with: Servier, MSD, Amgen, Novartis, Roche and Lilly

**OC5**

**SYSTEMIC TREATMENT WITH STRONTIUM RANELATE MARKEDLY IMPROVES THE HEALING OF CRITICAL BONE DEFECT**

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**Aims:** Rapid bone defect filling with normal bone is a challenge in orthopaedics (traumatology and oncology) and dentistry (tooth extraction). The classical strategy is to locally provide drugs and/or bone growth supports. Systemic treatment with antosteoporotic agent able to stimulate bone formation may be potentially useful. Healing of a critical bone defects is a model associating a phase of bone resorption (simultaneous with bleeding and inflammation) and of bone formation. Strontium ranelate which has been shown to decrease bone resorption and to positively influence bone formation, represents a potential agent able to stimulate bone defect filling.

**Methods:** To further explore this question, we set up a model of critical bone defect performed at the level of the rat proximal tibia. A drilling of 2.5 mm in diameter was created in the secondary spongiosa in 6 month-old female rats which were given strontium ranelate (625 mg/kg/d, 5/7 days) or vehicle for 4, 8 or 12 weeks (10 rats per group and per time point) starting at the moment of the surgery. The tibias were removed for microtomographic histomorphometry at the level of the healing bone defect at each time point. All results are expressed as means ± SEM. One-way ANOVA with a Fisher post-test was used to analyze the data (**\(p<0.01\) vs. time-control).

**Results:**

<table>
<thead>
<tr>
<th>Trabecular</th>
<th>Weeks</th>
<th>4</th>
<th>8</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>bone volume (%)</td>
<td>Controls</td>
<td>10.3±3.0</td>
<td>4.8±1.3</td>
<td>7.8±2.0</td>
</tr>
<tr>
<td></td>
<td>Strontium ranelate</td>
<td>17.7±3.5</td>
<td>16.3±2.4**</td>
<td>20.9±2.8**</td>
</tr>
<tr>
<td>thickness (mm)</td>
<td>Controls</td>
<td>0.066±0.005</td>
<td>0.062±0.003</td>
<td>0.064±0.005</td>
</tr>
<tr>
<td></td>
<td>Strontium ranelate</td>
<td>0.075±0.005</td>
<td>0.081±0.002**</td>
<td>0.082±0.002**</td>
</tr>
<tr>
<td>SMI</td>
<td>Controls</td>
<td>2.78±0.27</td>
<td>3.30±0.24</td>
<td>2.88±0.30</td>
</tr>
<tr>
<td></td>
<td>Strontium ranelate</td>
<td>2.25±0.28</td>
<td>2.14±0.13**</td>
<td>1.91±0.23**</td>
</tr>
</tbody>
</table>

Similar positive effects were observed for the other parameters evaluated by \(\mu\)CT like trabecular number and space. Strontium ranelate treatment induced an early increase of trabecular bone mass already visible by 4 weeks. This was associated with improvement of the microarchitecture with a significant thickening of the trabeculae visible after 4 weeks of treatment and increasing progressively, illustrating the potential benefit of strontium ranelate on bone formation. Finally as evaluated by SMI (3 = rodlike, 1 = platelike) trabeculae are more plate-like (optimal structure for mechanical resistance) in strontium ranelate treated rats than in control (rodlike).

**Conclusions:** Strontium ranelate represents a potential intervention to accelerate and enhance the filling of a bone defect, with potential advantages in dental or orthopedic-surgery for bone healing after tooth extraction and for implant osseointegration.

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OC6
FACTORS AFFECTING BMD IN YOUNG NEW
ZEALAND WOMEN OF INDIAN, CHINESE
AND CAUCASIAN ETHNICITIES
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Aims: To investigate the bone health of young women (19–29 years) of Indian and Chinese ethnicity living in Auckland, New Zealand, and the factors affecting the achievement of peak bone mass. A cohort of Caucasian women was recruited for the purpose of comparison.

Methods: We compared the lumbar spine and total hip bone density (BMD), serum 25(OH)D, calcium intake (4-day food diary), dairy intake (food frequency questionnaire) and physical activity of 137 New Zealand women aged 19–29 years, of Caucasian (n=79), Chinese (n=28) and Indian (n=30) ethnicity. Dairy consumption and physical activity (PA) during childhood and adolescence were also investigated.

Results: BMD was significantly lower in both the Chinese and Indian women with a high proportion meeting the diagnostic criteria for osteopenia (T-score ≤–1.0) in the hip (53 and 40%) and the spine (32 and 40%). Regression analysis identified BMI as the most significant predictor of BMD. Serum 25(OH)D was predictive only of spine BMD, and dietary calcium and PA predictive only of hip BMD. Mean 25(OH)D concentration and calcium intake were adequate only in the Caucasian women, and PA was lower in the Chinese and Indian women than in the Caucasian women (Table 1). Adult consumption of calcium-containing foods and patterns of PA correlated with behaviour during childhood and adolescence.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Caucasian (n=79)</th>
<th>Chinese (n=28)</th>
<th>Indian (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.5±2.7</td>
<td>24.3±2.7</td>
<td>24.2±2.6</td>
<td>NSD</td>
</tr>
<tr>
<td>BMI kg/m2</td>
<td>23.3±4.1</td>
<td>20.3±2.0</td>
<td>22.8±4.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Lumbar spine BMD (g/cm2)</td>
<td>1.040±0.122</td>
<td>0.960±0.107</td>
<td>0.968±0.087</td>
<td>0.001</td>
</tr>
<tr>
<td>Total hip BMD (g/cm2)</td>
<td>0.944±0.120</td>
<td>0.844±0.096</td>
<td>0.851±0.109</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum 25(OH)D (nmol/l)</td>
<td>63.5(10.0, 87.0)</td>
<td>38.0(28.0, 52.5)</td>
<td>26.0(13.0, 40.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Parathyroid Hormone (pg/ml)</td>
<td>3.04±0.91</td>
<td>3.90±1.65</td>
<td>4.66±1.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dietary calcium (mg)</td>
<td>989 (777, 1263)</td>
<td>539 (440, 704)</td>
<td>825 (504, 1207)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recreational physical activity (Hours/day)</td>
<td>0.85 (0.47, 1.42)</td>
<td>0.48 (0.15, 0.78)</td>
<td>0.38 (0.18, 0.82)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Differences between groups were determined by ANOVA with post hoc analysis (Tukey’s) for parametric data (log values were used for calcium) or Kruskall Wallis test with post hoc analysis (Bonferoni) for non-parametric data. Normally distributed data is expressed as mean ± SD, non-parametric data as median (25th, 75th percentiles). Different superscript numbers indicate significant difference.

Conclusions: The findings of this study demonstrate a cause for concern about the bone health of young New Zealand women, especially those of Asian or Indian ethnicity who were more likely to have lower BMI, serum 25(OH)D, dietary calcium and levels of physical activity in both childhood and as adults. Adult dairy consumption and PA, both important predictors of bone health, were shown to be significantly and positively related to behavioural patterns during childhood and adolescence, emphasising the importance of establishing good diet and lifestyle patterns early in life.

Disclosure of Interest: None Declared

OC7
A RANDOMIZED TRIAL OF BALLOON KYPHOPLASTY AND NONSURGICAL CARE FOR PATIENTS WITH ACUTE VERTEBRAL COMPRESSION FRACTURES: TWO YEAR RESULTS
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Aims: Balloon kyphoplasty is a minimally invasive treatment for acute vertebral fractures that aims to reduce and correct vertebral deformity by inserting expandable balloon tamps and then stabilize the body by filling it with bone cement. We tested the effects of balloon kyphoplasty on quality of life and anatomic correction of the vertebral body in a randomized trial.

Methods: Patients with up to 3 non-traumatic acute vertebral compression fractures were enrolled within 3 months of diagnosis and randomly assigned to receive either balloon kyphoplasty (N=149) or usual nonsurgical care (N=151). Measurements of quality of life, back pain and function, days of disability and spine radiographs were assessed through 24 months of follow-up.

Results: The mean SF-36 physical component summary (PCS) score improved 5.1 points (95%CI, 2.8–7.4; p<0.0001) more in the kyphoplasty than the nonsurgical group at 1 month, the primary endpoint of the study. Kyphoplasty...
improved the PCS score by an average of 3.0 points (95% CI, 1.6–5.4; \( p=0.002 \)) during the two-year follow-up. There was a significant interaction between treatment and follow-up time (\( p=0.003 \)), indicating that the treatment effect over the year is not uniform across follow-up; a result from early improvement that persists in the kyphoplasty group whereas the nonsurgical group shows more incremental improvement over time. Kyphoplasty resulted in more pain relief on a 0 to 10-point numeric rating scale (1.5 points; 95% CI 1.0–1.9; \( p<0.0001 \)), less Roland-Morris back disability (2.9 points; 95% CI, 1.6–4.1; \( p<0.0001 \)) and 2.2 (95% CI 1.1–3.7; \( p=0.0008 \)) fewer days of limited activity (within a two-week period) when averaged over 2 years. The postoperative mean change from baseline showed an average improvement of 3.3° (95% CI 2.4–4.2; \( p<0.0001 \)) correction in index fracture kyphotic angulation; correction was maintained over follow-up. At 24 months, there was an average 3.1° of correction in the kyphoplasty group compared to 0.8° in the control group (\( p=0.003 \) for comparison). There was no significant difference in the number of patients with adverse events or serious adverse events in the kyphoplasty and nonsurgical groups. There were two device-related serious adverse events in the second year that occurred at index vertebrae (a spondylitis and an anterior cement migration). There was no statistically significant difference between groups in the number of patients (47.5% for kyphoplasty; 44.1% for control) with new radiographic vertebral fractures; fewer fractures occurred (~18%) within the second year.

Conclusions: Compared to nonsurgical care, balloon kyphoplasty improved quality of life, reduced back pain and disability and improved vertebral body kyphosis correction and did not increase adverse events including the risk of vertebral fracture over 2 years.


OC8

FREEDOM TRIAL FIRST-YEAR EXTENSION: RESULTS FROM 4 YEARS OF DENOSUMAB EXPOSURE IN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS


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Aims: To investigate the long-term efficacy and safety of denosumab (DMAb) for the treatment of postmenopausal women with osteoporosis in an open-label extension to the 3-year FREEDOM study.1

Methods: All women who completed the FREEDOM study were eligible to enter a long-term open-label extension (up to 10 years). After providing informed consent, participants received 6-monthly subcutaneous injections of DMAb (60 mg). Here we report data from the first year of follow-up. For women randomized to DMAb in the FREEDOM study (‘long-term group’), this represents up to 48 months of DMAb exposure (eight 6-monthly injections). For those randomized to placebo (‘de novo group’) the data are from up to 12 months of exposure (two injections). All participants continued to take calcium (1 g) and vitamin D (≥400 IU) supplements daily. Changes in bone mineral density (BMD) and bone turnover markers (BTM) are reported for subjects enrolled in the extension. No formal statistical testing was planned for this interim report. P-values are descriptive.

Results: Overall, 4,550 eligible women (70.2%) who completed the FREEDOM study entered the open-label extension study (long-term, n=2,343; de novo, n=2,207). During the first year of the extension, lumbar spine (LS) BMD in the long-term group further increased by 2.0% (12.1% increase vs. FREEDOM baseline at 48 months), and total hip (TH) BMD further increased by 0.8% (6.5% increase at 48 months) (\( p<0.0001 \)) for both BMD gains during year 4; Fig. 1). During the first year of the extension, LS and TH BMD increased by 5.4% and 3.0%, respectively, in the de novo group (both \( p<0.0001 \)). After DMAb initiation, serum C-telopeptide (CTX) in the de novo group decreased rapidly and similarly to the long-term group (Fig. 2). Reductions in BTMs continue to attenuate at the end of the dosing interval as previously reported. Adverse event (AE) rates were similar (70.4% of women in the long-term group and 67.9% in the de novo group). Serious AEs were also similar (9.8% and 11.2% of women, respectively). During year 4, osteoporotic nonvertebral fractures were
reported in 31 women in the long-term group and 51 in the de-novo group.

**Fig. 1.** Percentage change in BMD with denosumab for 4 years (long-term) or 1 year (de novo)

![Lumbar Spine BMD](image)

![Total Hip BMD](image)

**Conclusions:** These interim results suggest that continuation of DMAb treatment through 48 months is associated with further significant increases in spine and hip BMD with sustained reduction of bone turnover. The de-novo treatment group results confirm the first year active treatment findings previously reported¹.


**Acknowledgements:** Amgen Inc. sponsored this study. Figure ©2010, American Society for Bone and Mineral Research, used by permission, all rights reserved.


**Fig. 2.** Percentage change in sCTX over time

![Percentage change in sCTX over time](image)

* = Month 36 Day 10, Month 39 and Month 40 visits
**OC9**

**RONACALERET, A CALCIUM-SENSING RECEPTOR ANTAGONIST, INCREASES TRABECULAR BUT NOT CORTICAL BMD BY QCT IN POSTMENOPAUSAL WOMEN**

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**Aims:** Ronacaleret (RON) is a calcilytic compound that stimulates parathyroid hormone (PTH) release from the parathyroid cell. The aims of this study were to determine optimum dosing regimens of RON for improvement in bone mineral density (BMD) by DXA, and to evaluate the distribution of BMD changes by QCT in postmenopausal women with osteoporosis or osteopenia.

**Methods:** In a phase II double-blind, placebo-controlled, dose-ranging study, 569 postmenopausal women with osteoporosis or osteopenia were enrolled to open-label teriparatide dose-ranging study, 569 postmenopausal women with osteo-

**Results:** Lumbar spine (LS) aBMD had modest but statistically significant increases by DXA (1.4–1.9%; 200–400 mg) in the RON dose groups compared to larger increases with ALN (4.7%) and TER (9.2%) compared to baseline. RON administration resulted in a decrease in total hip aBMD by DXA (−0.6 to −1.2%) and increases with ALN (2.8%) and TER (2.6%). A subset of subjects had QCT of the hip and spine performed. Vertebral integral vBMD at the LS revealed dose-dependent mean increase over baseline in the ronacaleret dose groups which, at RON 400 mg, was similar to the increases noted with ALN. LS trabecular vBMD was increased in the RON groups (13.3%, 400 mg) greater than that seen with ALN (4.9%). In contrast, cortical parameters (e.g., midvertebral cortical vBMD) had small non-dose-dependent increases over baseline in RON as compared to significant increases with ALN and TER. At the hip, RON resulted in slight, nonsignificant mean decreases from baseline in femur integral vBMD (−0.1 to −0.8%) compared to increases with ALN (2.7%) and TER (3.9%) compared to baseline. The femur cortical vBMD was unchanged from baseline in TER, increased with ALN (2.4%) and decreased in the RON dose groups (−0.3 to −1.8%). PTH levels were prolonged after administration of RON compared to TER historical controls. There was a mild increase in serum calcium levels with the administration of RON which returned to baseline after discontinuation of drug.

**Conclusions:** The nonsignificant small negative effects on cortical vBMD with RON were in contrast to the improvements in trabecular bone. We suggest that RON induced a mild primary hyperparathyroidism which resulted in preferential effects on trabecular bone compartments.

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**Disclosure of Interest:** L. Fitzpatrick Employee of: GlaxoSmithKline, C. Dabrowski Employee of: GlaxoSmithKline, G. Cicconetti Employee of: GlaxoSmithKline, D. Gordon Employee of: GlaxoSmithKline, T. Fuerst Consultant/Advisor of: Roche, Merck, Amgen, Lilly, Servier, BMS, Genentech, Stock ownership or royalties of: Synarc, Inc.

**OC10**

**EGB-761 IS A DUAL ACTION COMPOUND: INHIBITS BONE MARROW ADIPOGENESIS, ARTERIOSCLEROTIC PLAQUE FORMATION AND PROMOTES OSTEOBLASTOSTGENESIS**

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**Aims:** Aging process adversely affect both bone metabolism and vascular integrity leading to vascular calcification and low bone density. Therefore, we considered intervening with an agent that, can address both the issues of osteoporosis as well as arterial calcification.

**Methods:** The effects of standardized and concentrated extract of Ginko biloba, Egb-761 were studied on estrogen deficiency induced bone loss in ovariectomized rats. We have also investigated the anti-obesity and anti athero-sclerotic ability of Egb-761 in our in vitro and in vivo (high fat high cholesterol diet induced) model

**Results:** Oral administration of Egb-761 exhibited bone sparing effect which was reflected by better bone microarchitectural parameters compared with OVX + vehicle group. In the 3T3L1 preadipocyte cells Egb-761 effectively inhibited adipocyte differentiation via inhibition of expression of PPARγ, C-EBPα in 3T3L1 preadipocyte cells with activation of ROS an important upstream signal for stress induced apoptosis in cells. In vivo study to screen Egb-761’s hypolipidemic action
using Triton-WR-1339 (induces hyperlipidemia), Egb761 inhibited serum cholesterol and triglyceride levels, thus decelerating lipid biosynthesis leading to lipid catabolism. In the High Fat Diet (HFD) induced model, treatment with the high fat diet resulted in significantly higher plasma total cholesterol and high density lipoprotein cholesterol (HDL-C) levels. The same animals were fed Egb-761 at 50, 100 and 250 mg \(^{-1}\) kg \(^{-1}\) doses for 2 weeks. In the (HFD + Egb-761) treated group blood glucose concentrations were significantly lowered. Further a dose of 250 mg \(^{-1}\) kg \(^{-1}\) was decided to study the effect of Egb-761 on high fat high cholesterol diet (HFFCD) in the hamster model that are susceptible to atherosclerosis and lipid oxidation. HFCFD was fed for up to 4 weeks followed by treatment with Egb-761 for 4 weeks.

**Conclusions:** Our data with HFCD shows that Egb-761 treatment leads to improvement in total cholesterol and LDL cholesterol levels as compared to the HFCDF control group. Overall our results demonstrate that oral administration of Egb-761 not only leads to vascular preservation of the aortic lumen with impairment of the endothelium dependent relaxation but also restores bone mass in aged OVX rats.

**Disclosure of Interest:** None Declared

**OC11**

**RAPIDLY INCREASING RATES OF HIP FRACTURE IN BEIJING, CHINA: A POPULATION-BASED STUDY WITH VALIDATED RATES**

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**Aims:** To explore the change of the hip fracture incidence of Beijing in the last decade.

**Methods:** We replicated the methods of a 1990-1992 population-based study of hip fractures in Beijing, China. Hospital discharge data for 2002-2006 were collected for all Beijing hospitals that admit hip fracture patients. Discharge lists were compared with original medical records, radiology, or operative reports in a stratified random sample of the hospitals and estimated hip fracture rates were adjusted for estimated rates of under- and over-reporting. The population of Beijing was based on the 1990 and 2004 censuses.

**Results:** Public health records underestimated the number of hip fractures in 1990–1992 by 67% primarily because of systematic miscoding of intertrochanteric fractures. The public records overestimated the number of hip fracture cases in 2002–2006 by about 20% because it counted a large number of cases referred from outlying areas. After corrections, the age-specific rate of hip fracture increased during that interval increased by 82% for women age 70–75 years and 442% for women over age 85 years, with similar increases in older men. During the same interval, the population of Beijing over age 65 more than doubled and the ownership of automobiles increased from 4 to 18 per 100 adults.

**Conclusions:** Reports of temporal changes in hip fracture rates in developing countries may be inaccurate because of changes in methods of reporting and changes in patterns of referral. The age-specific rate of confirmed hip fracture is rising very rapidly in Beijing, China, in parallel with a major influx of elderly people and a shift to motor transportation. Consequently, the burden of hip fractures may be rapidly shifting from West to East.

**Acknowledgements:** This study was supported by a grant from The Ministry of Science and Technology of the People’s Republic of China (National Public Welfare Research Program 2005DIB1J085 and National Key Technology R&D Program 2006BAI03B03). The Beijing Public Health Information Center collected data from all of the hospitals in the random sample hospital. The authors also appreciate the statistical assistance of Professor Han Shaomei and Mr. Xu Tao, Department of Epidemiology and Statistics, Peking Union Medical College.

**Disclosure of Interest:** None Declared

**OC12**

**GENDER DIFFERENCES IN INCIDENCE OF FALLS AND ITS ASSOCIATED FACTORS IN A POPULATION-BASED COHORT STUDY IN JAPAN: THE ROAD STUDY**

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**Aims:** The aim of the present study was to analyze the variation in fall rate by gender and age strata, and to determine the association of anthropometric measurements, physical ability, radiographic osteoarthritis (OA) of the knee and lumbar spine, pain in the knee and lower back, and cognitive impairment, with single and multiple falls in Japan.

**Methods:** A questionnaire was used to evaluate the number of falls during the 12 months preceding the baseline survey. Knee and lumbar spine radiographs were evaluated using the Kellgren Lawrence (KL) system; radiographic knee OA and lumbar spondylosis were defined as KL=3 or 4. Physical ability was estimated by measuring grip strength, 6-m walking time, normal step length, and chair-stand time. Cognition was also assessed for all participants by using a mini-mental state examination.

**Results:** From the 1,690 participants in mountainous and seacoast cohorts in the ROAD study, we included 1,675 participants who provided complete questionnaires regarding falls (587 men and 1,088 women; mean age, 65.3±
12.0 years) in the present study. During 1 year, 79 (13.5%) men and 207 (19.0%) women reported at least one fall. Multiple fall rate increased with age in women (odds ratio (OR) 1.04, 95% CI, 1.02–1.06), while it decreased with age in elderly men over 60 years (OR 0.93, 95% CI 0.88–0.98) (Figure). Multinomial logistic regression analysis showed that 6-m walking time was significantly associated with single and multiple falls in men under 60 years (single falls: OR, 1.65; 95% CI, 1.08–2.52; multiple falls: OR, 1.71; 95% CI, 1.14–2.26). However, the findings differed in the case of men over 60 years (single falls: OR, 1.08; 95% CI, 0.90–1.23; multiple falls: OR, 1.01; 95% CI, 0.86–1.14). There were no other factors associated with falls in men. In women, age, height, body mass index (BMI), grip strength, 6-m walking time, normal step length, chair-stand time, radiographic knee OA and lumbar spondylosis, knee pain, lower back pain, and cognitive impairment were significantly associated with multiple falls as assessed by multinomial logistic regression analysis without adjustment (ORs, 1.04, 0.95, 1.10, 0.92, 1.10, 0.98, 1.06, 2.60, 2.52, 1.60, 2.14, and 3.86; 95% CIs, 1.02–1.06, 0.92–0.98, 1.03–1.17, 0.89–0.96, 1.02–1.17, 0.96–1.00, 1.02–1.10, 1.64–4.26, 1.58–4.02, 1.01–2.54, 1.30–3.46, and 1.67–3.83, respectively). However, there were no factors significantly associated with single falls except for weight (OR, 1.02; 95% CI, 1.00–1.04). After adjustment for all the variables, BMI, grip strength, and knee pain were found to be independently associated with multiple falls in women (ORs, 1.08, 0.92, and 1.87; 95% CIs, 1.00–1.16, 0.88–0.97, and 1.06–3.28, respectively).

Conclusions: The present study revealed gender differences with regard to fall rate and factors associated with multiple falls.

Disclosure of Interest: None Declared

OC13
HIP FRACTURE PATIENTS IN INDIA HAVE VITAMIN D DEFICIENCY AND SECONDARY HYPERPARATHYROIDISM
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Aims: Vitamin D deficiency has been reported to be an important risk factor for hip fracture among elderly from Japan, Finland, Spain and Italy. There is limited data on prevalence of vitamin D deficiency in hip fracture patients from Indian population. Therefore this case control study was done to evaluate the parameters of bone mineral homeostasis such as serum 25(OH)-D and intact parathyroid hormone (PTH) levels in patients with hip fracture from North India.

Methods: Ninety consecutive newly diagnosed patients with hip fracture admitted to Lok Nayak Hospital, Maulana Azad Medical College, New Delhi were enrolled in the study during a period from October 2008 to February 2010. Similar number of age, sex and co-morbid illness matched controls were also included in the study during the above period. The levels of serum 25(OH)-D, intact parathyroid hormone (intact PTH), alkaline phosphatase (ALP), albumin, serum calcium and serum phosphorus were examined in each group. HypovitaminosisD was defined as serum 25(OH)-D <20 ng/dl. The upper normal limit for serum intact PTH was taken as 54 pg/dl.

Results: The serum 25 (OH)-D, serum calcium and serum albumin levels were significantly lower in patients with hip fracture than in controls, whereas the intact PTH and ALP levels were significantly higher in patients with hip fracture. There was significant negative correlation between serum 25(OH)-D and intact PTH. In the hip fracture group, 76.7% of the subjects had hypovitaminosis D (25-OHD <20 ng/ml) and 68.9% had elevated PTH levels (>54 pg/ml). On comparison 32.3% of the controls had vitamin D deficiency and 42.2% had elevated PTH levels. These differences were statistically significant.

Conclusions: Our results indicate that about three-fourths (76.7%) of hip fracture patients had vitamin D deficiency, whereas about two-thirds had secondary hyperparathyroidism suggesting that these conditions may be closely associated with hip fracture in elderly people. Therefore, the serum 25 (OH)-D level may be a useful index for the assessment of risk of hip fracture in elderly people.

Disclosure of Interest: None Declared

OC14
EFFECT OF CALCIUM AND VITAMIN D FORTIFIED CEREAL-BASED FOOD SUPPLEMENT ON THE BONE HEALTH AMONG SRI LANKAN PRE-SCHOOL CHILDREN
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Aims: Vitamin D deficiency has been reported to be an important risk factor for hip fracture among elderly from Japan, Finland, Spain and Italy. There is limited data on prevalence of vitamin D deficiency in hip fracture patients from Indian population. Therefore this case control study was done to evaluate the parameters of bone mineral homeostasis such as serum 25(OH)-D and intact parathyroid hormone (PTH) levels in patients with hip fracture from North India.
Aims: To assess the effectiveness of calcium and vitamin D₃ in the fortified food supplement named ‘Thriposha’ (a ready to eat cereal based supplement) on bone mineralization among preschool children aged 3–5 years.

Methods: Subjects in the interventional group (n=30) were fed with conventional Thriposha while children in the control group (n=30) were fed with Thriposha made without mineral and vitamin premix for a period of 9 months. Bone mineral density (BMD) and content (BMC) of the total spine were assessed using a dual-energy X-ray absorptiometry (Hologic discovery) at the baseline and after supplementation together with the serum parameters of calcium and vitamin D.

Results: Of thirty children included in each group, there were 15 males in the interventional group and 14 in the control group. There was no difference in age distribution (p=0.17) of these two groups. Mean (SD) ages of interventional and control groups were 48.2 (7.2) and 49.3 (7.1) months. The mean (SD) baseline total spine BMD was 0.464(0.050) g/cm² in the interventional group and 0.453(0.035) g/cm² in the control group (p=0.09). The total spine BMC and bone area of the interventional group were 11.68(1.90) g and 25.12(SD) cm², respectively whereas the corresponding values in the control group were 11.14(1.70) g (p=0.24) and 25.12 (2.43) cm² (p=0.86), respectively. Total spine BMD Z-score at baseline in the interventional group was significantly higher (p<0.05) when compared with the control group (−0.13 vs. −0.79).

The mean total spine BMD and Z-score of the interventional group children showed a significant improvement over the control group children (total spine BMD level of 0.487(0.047) g/cm² vs. 0.454(0.031) g/cm²; p (for between group difference) <0.001) and total spine Z-score (−0.030 (0.82) vs. −0.823 (0.69); p (for between group difference) = 0.005) among interventional and control group children respectively after the intervention. The effect of Thriposha supplementation on biochemical parameters are summarized in the table.

Table Effect of supplementation on serum calcium and vitamin D³

<table>
<thead>
<tr>
<th></th>
<th>Interventional</th>
<th></th>
<th>Control</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Final</td>
<td>Baseline</td>
<td>Final</td>
</tr>
<tr>
<td>Serum Calcium (mmol/l)</td>
<td>1.95 (0.5)</td>
<td>2.49(0.5)</td>
<td>1.94(0.3)</td>
<td>1.72(0.5)</td>
</tr>
<tr>
<td>difference</td>
<td>+0.5(0.1)</td>
<td></td>
<td>−0.2(0.1)</td>
<td></td>
</tr>
<tr>
<td>Serum Vitamin D (mmol/l)</td>
<td>71.95(32.3)</td>
<td>96.28(27.5)</td>
<td>103.44(26.4)</td>
<td>96.30(36.9)</td>
</tr>
<tr>
<td>difference</td>
<td>+24.3(6.5)</td>
<td></td>
<td>−7.1(7.3)</td>
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</tr>
</tbody>
</table>

Results expressed in mean (SD) where as difference was given as mean (SEM). There was a significant difference (p<0.05) in serum vitamin D levels at baseline.

Conclusion: This study showed that calcium containing Thriposha supplement influences bone mass acquisition, leading to a higher peak bone mass. These results imply that standards for dietary calcium and vitamin D intake in childhood should be based on growth rate as well as bone size development.

Disclosure of Interest: None Declared

OC15

COMPARISON OF THE THERAPEUTIC EFFECT OF TERIPARATIDE WITH THAT OF ANTiresORPTIVE AGENTS FOR THE TREATMENT OF NEW-ONSET ADJACENT VERTEBRAL COMPRESSION FRACTURE AFTER PERCUTANEOUS VERTEBROPLASTY

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Aims: Percutaneous vertebroplasty may provoke fractures in adjacent, non-augmented vertebrae. Subsequent VCFs can occur much sooner and more frequently after PVPs. Antiresorptive agents do not provide prompt pain relief or effectively prevent new-onset VCFs. Teriparatide is effective in increasing spinal bone mineral density (BMD) and in decreasing vertebral fracture risk in patients with osteoporosis. This comparative study is aimed to evaluate the effectiveness of teriparatide for treating new-onset adjacent VCFs after vertebroplasty.

Methods: In the prospective group (group A), we enrolled 32 patients who were treated with teriparatide for new-onset adjacent VCFs following PVP. Data in group A, including visual analogue scale (VAS) scores and BMD were compared with those in a retrospective group (group B) of 33 patients who received antiresorptive agents and repeated PVPs for new-onset VCFs.

Results: In group A, one new-onset adjacent compression fracture occurred during the mean follow-up period of 22.56 months. In group B, five patients (6 vertebrae) developed new-onset VCFs after the second PVP, and two of these five patients had additional new VCFs after the third PVP. Teriparatide reduced the risk for new VCFs by 79.33% (Figure A). The lumbar spine BMD increase was 27.63% after 18 months of treatment with teriparatide and 4.62% after 18 months of
treatment with antiresorptive agents (Figure C). In addition, at 18-month follow-up, mean VAS scores had decreased from 8.03±1.97 to 1.37±0.52 in the teriparatide group and from 7.91±1.95 to 4.23±1.21 in the antiresorptive group (Figure B).

**Conclusions:** Teriparatide treatment of new VCFs after vertebroplasty is effective for pain relief and preventing new-onset VCFs.

**Disclosure of Interest:** None Declared