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glucocorticoid-induced OP. Authors from the UK reported high persistence rate with TPTD: 87% of postmenopausal women and 81.4% of men were still on treatment after 12 months. A recent French study confirmed a high persistence rate for patients receiving an education and follow-up program (81.5% at 15 months).

**Aim:** To evaluate the persistence with TPTD in northern Italy patients with severe OP.

**Methods:** A total of 296 patients (270 females and 26 males) were followed up for a period of 3–18 months (mean 9 months) during teriparatide treatment. When starting TPTD the patients were aged 42–91 years and had at least two vertebral fractures. Persistence with treatment and causes for discontinuation were evaluated.

**Results:** After a mean observation period of 9 months 259 patients were still on treatment (persistence rate 87.5%), while 37 patients (12.5%) dropped-out: 25 patients (68%) stopped the treatment prematurely due to adverse events and 12 patients (32%) were lost at follow-up. Causes for premature discontinuation were: nausea/vomiting (10 patients), back pain/arthralgia (3), vertigo/dizziness (3), tachycardia (2), pruritus (2), abdominal pain (1), hypercalcemia (1), leg cramps (1), others (4).

One-hundred and eighteen patients (40%) were followed for the whole 18-month observation period: 101 patients completed the 18-month treatment course (persistence rate 86%), while 16 patients dropped-out (9 patients for adverse events and 8 patients lost at follow-up).

**Conclusion:** According to literature data, our preliminary results from northern Italy show that patients with severe OP treated with TPTD have a high persistence over the 18-month course of treatment.

**Conflict of interest:** None declared.

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#### P480

##### The efficacy of parathyroid hormone in improving health related quality of life in severe osteoporotic patients

M. Bentivegna\*

ASL 7 Ragusa, Ambulatorio di Reumatologia e Osteoporosi, Ragusa, Italy

Osteoporosis is a systemic skeletal disease characterized by a low bone mass and bone architectural derangements, leading to an increased fracture risk [1]. It has been previously demonstrated that affected patients perceive osteoporosis as a disease leading to discomfort, disability and to an impaired quality of life [2].

We have reviewed the database of our patients treated with full-length parathyroid hormone (PTH 1–84), an osteoanabolic agent that has demonstrated its efficacy in preventing fractures and increasing bone mineral density, in the TOP pivotal trial [3]. Our hypothesis was that PTH 1–84 might also improve the health related quality of life (HRQOL), as previously described with the PTH analogue teriparatide. We have analyzed our database of patients with severe osteoporosis and treated with PTH 1–84. We identified 16 patients affected by severe postmenopausal osteoporosis (average age  $73.3 \pm 7.2$ ), treated for 12 months with PTH 1–84. As per our clinical practice we have assessed HRQOL with 2 different tools: QUALEFFO 41 and a Visual Analogue Score (VAS). The latter is a self-evaluation of the global muscle-skeletal discomfort intensity; in both cases the higher is the score the worse is the HRQOL.

A Wilcoxon test was performed in order to compare scores of both tools before and after the treatment (mean  $\pm$  SD). There was a significant improvement of both QUALEFFO total score ( $60.1 \pm 13.6$  baseline;  $57.6 \pm 12.2$  at month 12;  $p < 0.01$ ) and VAS score ( $7.41 \pm 1.0$  baseline;  $6.6 \pm 1.6$  at month 12;  $p < 0.05$ ).

Our clinical experience indicates that PTH 1–84 has a positive impact on the patients' perceived quality of life.

1. World Health Organization (WHO) Working Group: Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. WHO Technical Report Series 843, Geneva: WHO; 1994.

2. Bianchi M.L et al. Health and Quality of life outcomes 2005, 3:78.

3. Greenspan et al. Ann Intern Med 2007, 146, 326–339.

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#### P481

##### Kalsis, a food supplement, decreases the ovariectomy-induced osteopenia in rats

M. Montero<sup>a,\*</sup>, M. Diaz-Curiel<sup>b</sup>, S. Dapia<sup>c</sup>, J. Caeiro<sup>d</sup>, C. De la Piedra<sup>e</sup>

<sup>a</sup>Laboratorio de Fisiopatología Osea, Madrid, Spain

<sup>b</sup>Medicina Interna, Fundación Jiménez Díaz, Madrid, Spain

<sup>c</sup>Trabeculae® Empresa de Base Tecnológica S.L., Parque Tecnológico de Galicia, San Cibrao das Viñas, Ourense, Spain

<sup>d</sup>Servicio de Cirugía Ortopédica y Traumatología, Complejo Hospitalario Universitario de Santiago de Compostela, A Coruña, Spain

<sup>e</sup>Servicio de Bioquímica, Laboratorio de Fisiopatología Osea, Fundación Jiménez Díaz, Madrid, Spain

There are evidence about the fact that the administration of Kalsis (Catalysis Labs, Spain), a food supplement that contains selenium, to postmenopausal-osteoporosis women, produces an increase in bone mass. According to the manufacturer, the different compounds of supplement are activated through molecular-activation principles which strongly increase their biological activity without any modification in their structure. The aim of this work was to study the ability of Kalsis to prevent the effects of ovariectomy on bone loss. Thirty-six, 6-month-old, Wistar female rats were SHAM-operated or ovariectomized.

Groups: SHAM: sham-operated rats and OVX: ovariectomized rats treated with vehicle (water, 0.3 mL/rat/day); OVX + Kalsis: ovariectomized rats treated with Kalsis (25 mg/kg/day). Treatment was administered for 3 months by oral gavage, beginning one day after surgery. Animals were killed and bone mineral density (BMD) was determined by DXA in the lumbar spine and in the whole left femur. Computerized microtomography (microCT) in femur by Skyscan 1172 (Trabeculae®, Empresa de Base Tecnológica S.L.), and serum osteocalcin (BGP), aminoterminal propeptide of procollagen I (PINP), beta-isomer of carboxyterminal telopeptide of collagen I (beta-CTX) and 5b isoenzyme of ttrate-resistant acid-phosphatase (TRAP) were performed.

OVX group presented values of lumbar and femoral BMD lower than the SHAM group. Treatment with Kalsis prevented the loss of BMD due to ovariectomy. Results from microCT showed a decrease in BV/TV, and trabecular number, and an increase in trabecular separation without changes in trabecular thickness in OVX rats. Kalsis treatment avoided partially this decrease in BV/TV and the increase in trabecular separation showing an increase in trabecular thickness with respect to SHAM and OVX groups. Ovariectomy increased levels of biochemical markers of bone formation (BGP and PINP) and the resorption index (CTX/TRAP). Treatment with Kalsis maintained this increase with respect to SHAM group.

The above results suggest that Kalsis administration partially avoided the development of osteopenia due to estrogen lack. The mechanism of action of this supplement is not produced through a decrease in bone remodelling rate because levels of bone formation and resorption are increased in the treated animals. The anti-oxidant action of selenium as a cause of this beneficial effect is suggested.

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#### P482

##### Odanacatib treatment in postmenopausal women with low bone mineral density: 24-month results

M. McClung<sup>a,\*</sup>, J.A. Eisman<sup>b</sup>, H.G. Bone<sup>c</sup>, C. Roux<sup>d</sup>, R.R. Recker<sup>e</sup>, N. Verbruggen<sup>f</sup>, C.M. Hustad<sup>g</sup>, C. daSilva<sup>h</sup>, D. Kimmeli<sup>i</sup>, A. Santora<sup>h</sup>, A. Ince<sup>a</sup>

<sup>a</sup>Research, Oregon Osteoporosis Center, Portland, USA

<sup>b</sup>Research, Garvan Institute of Medical Research, Sydney, Australia

<sup>c</sup>Research, Michigan Bone and Mineral Center, Detroit, USA

<sup>d</sup>Research, Cochin Hospital, University of Paris, Paris, France

<sup>e</sup>Research, School of Medicine, Creighton University, Omaha, USA

<sup>f</sup>Statistics, Merck and Co., Inc., Brussels, Belgium

<sup>g</sup>MRL, Merck and Co., Inc., North Wales, USA

<sup>h</sup>Research, Merck and Co., Inc., Rahway, USA

<sup>i</sup>Research, Merck and Co., Inc., West Point, USA

<sup>j</sup>MRL, Merck and Co., Inc., Rahway, USA

**Background:** Odanacatib (MK-822) is a selective inhibitor of cathepsin K shown to rapidly and reversibly decrease bone resorption in preclinical and Phase I studies.

**Methods:** A randomized, double-blind, 2-year study (1-year base + 1-year extension) was performed in postmenopausal women with low BMD to evaluate the safety and efficacy vs. placebo of 3, 10, 25 or 50 mg weekly of odanacatib on BMD, bone turnover markers, and histomorphometry. Postmenopausal women ( $N=399$ , mean age:  $64.2 \pm 7.8$  years) with BMD  $T$ -scores  $<2.0$  at the lumbar spine, total hip, femoral neck or hip trochanter and  $>3.5$  at all sites were randomized to receive placebo or 1 of 4 doses of odanacatib. 320 women continued into the extension, and 280 women completed 2 years of treatment; sponsor was unblinded to allocation in the extension. Trabecular bone turnover was assessed via transilial biopsies obtained from all consenting participants at 24 months. The primary endpoint was % change vs. baseline in lumbar spine BMD.

**Results:** There were progressive dose-related increases in BMD vs. baseline. Lumbar spine and total hip BMD increased 5.5% and 3.2%, respectively, with the 50-mg dose and were essentially unchanged with placebo ( $-0.2\%$  and  $-0.9\%$ ). Urinary N-telopeptides (NTx/Cr) and bone-specific alkaline phosphatase (BSAP) decreased 52% and 13%, respectively, with the 50-mg dose, whereas uNTx/Cr decreased 5% and BSAP increased 3% with placebo. There were no dose-related trends in AEs. Preliminary transilial biopsies ( $N=27$ ) indicated no significant effect on bone remodeling.

**Conclusion:** Odanacatib treatment for 24 months in postmenopausal women with low BMD increased lumbar spine and total hip BMD with no evidence of skeletal toxicity.

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#### P483

##### Further reductions in bone turnover after transition from alendronate to denosumab in ovariectomized cynomolgus monkeys resulted in maintained or improved cortical and trabecular bone mass and bone strength

M.S. Ominsky<sup>a,\*</sup>, S.Y. Smith<sup>b</sup>, J. Jolette<sup>b</sup>, F. Vlasseros<sup>b</sup>, R. Samadfam<sup>b</sup>, P.J. Kostenuik<sup>a</sup>

<sup>a</sup>Metabolic Disorders, Amgen Inc., Thousand Oaks, USA

<sup>b</sup>Charles River Laboratories, Preclinical Services Montreal Inc., Montreal, PQ, Canada

The safety and efficacy of transitioning from a bisphosphonate to denosumab (DMAB, a fully human RANKL antibody) were examined in ovariectomized (OVX) cynomolgus monkeys (cynos). Adult OVX cynos were treated with vehicle (Veh,  $n=20$ ), alendronate (ALN,  $n=21$ ; 50  $\mu\text{g}/\text{kg}$  IV biweekly), or DMAB ( $n=11$ ; 25  $\text{mg}/\text{kg}$  SC monthly). After 6 mos, 10 Veh and 11 ALN treated animals were switched to 6 mos of treatment with DMAB (Veh-DMAB and ALN-DMAB), while the other animals remained on their original treatment. Transition from ALN to DMAB revealed no safety concerns, including no significant alterations in serum calcium. DMAB and ALN significantly reduced serum CTx and osteocalcin, with further reductions after transition from ALN to DMAB. Dynamic histomorphometry at trabecular and cortical sites demonstrated significant reductions in bone turnover parameters after 12 mos of DMAB or ALN. Turnover suppression with DMAB or ALN-DMAB was greater than with ALN alone for most parameters. Cortical porosity at the rib and tibia was significantly lower with DMAB and with ALN-DMAB ( $p < 0.05$  vs. Veh), but not with ALN alone. BMD at cancellous (lumbar spine) and cortical (tibia diaphysis) sites was significantly increased by ALN and DMAB, and continued to increase at both sites after transition from ALN to DMAB. Vertebral trabecular core peak load and stiffness were significantly greater in DMAB and ALN-DMAB groups ( $p < 0.05$  vs. Veh), but not in the ALN alone group. No significant differences were found in extrinsic bone strength parameters at the femur neck and femur diaphysis, or in intrinsic strength parameters derived from the femur diaphysis for any group. Maintenance of normal material properties was also demonstrated by strong and similar positive correlations within and across each group for load versus BMC at the femur diaphysis (overall  $r^2=0.80$ ), femur neck ( $r^2=0.53$ ), vertebral bodies ( $r^2=0.69$ ), and vertebral trabecular cores ( $r^2=0.83$ ). In OVX cynos, transition from ALN to DMAB had a similar safety profile to continued ALN and resulted in further reductions in bone turnover while maintaining or improving cortical and trabecular bone mass and strength. The linear relationship between bone mass and strength was preserved in all groups, suggesting that bone mass predicted bone strength independent of these treatment regimens.

**Conflict of interest:** MS Ominsky, Amgen Inc., employee and shareholder. SY Smith, Amgen Inc., paid contractor. J Jolette, Amgen

Variable	Units	Placebo	Odanacatib			
		N=6	3 mg N=7	10 mg N=5	25 mg N=6	50 mg N=4
Bone formation (surface)	$\mu\text{m}^3/\mu\text{m}^2/\text{d}$	$0.037 \pm 0.011$	$0.049 \pm 0.010$	$0.017 \pm 0.005$	$0.027 \pm 0.006$	$0.033 \pm 0.014^a$
Activation frequency	/yr	$0.50 \pm 0.16$	$0.66 \pm 0.15$	$0.24 \pm 0.07$	$0.34 \pm 0.07$	$0.42 \pm 0.17^a$
Osteoclast surface/bone surface	%	$0.62 \pm 0.18$	$0.58 \pm 0.15$	$0.43 \pm 0.16$	$0.59 \pm 0.10$	$0.43 \pm 0.25$
Mineralizing/osteroid surface	%	$63 \pm 18$	$82 \pm 22$	$54 \pm 11$	$63 \pm 11$	$32 \pm 12$
Mineralization lag time	days	$27 \pm 8$	$178 \pm 3$	$19 \pm 5$	$15 \pm 2$	

All values are mean  $\pm$  standard error.

<sup>a</sup>  $N=3$  for these endpoints in this group.