osteoporotic women (56 without and 44 with previous fracture), using DXA performed on Discovery TM osteodensitometer (Hologic, Bedford, MA). Fracture risk assessment tool (FRAX index) for major osteoporotic and hip fractures was calculated based on demographic data and BMD hip value. HRQoL was assessed using QUALEFFO-41 questionnaire (domains: health perception, pain, physical, social and mental function).

Results: Basic characteristics of participants (age, length of menopause, BMI, smoking habit, hereditary tendency to fractures, fracture history) correlated with some QUALEFFO-41 domains, but coefficients of correlation were low ($r < 0.3$), except in case of pain domain to fracture history relationship ($r = 0.638$). Out of those six chosen predictable variables in the multiple regression model, fracture history was shown to be the most significant predictable variable for three QUALEFFO-41 domains: pain ($b = 20.511$), social function ($b = 2.548$) and health perception ($b = 3.185$). Correlation analysis showed that, after adjustment for basic characteristics of subjects, the strongest correlations were found between BMD and T-score at femoral neck and pain ($r = 0.331$ and $r = 0.449$, respectively), social function ($r = 0.422$ and $r = 0.419$) and health perception domains ($r = 0.434$ for T-score at femoral neck).

Conclusion: The results of our study confirm previously established relationship between BMD at femoral neck and HRQoL in patients with osteoporosis.

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THE WNT-INACTIVATING LIPASE NOTUM AS A NOVEL ANABOLIC OSTEOPOROSIS DRUG TARGET

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To identify novel osteoporosis drug targets, Lexicon's gene knockout (KO) phenotyping campaign (≈4,650 distinct genes) included DXA measurements of body, spine and femur BMD plus microCT analyses of trabecular (LV5) and cortical (midshaft femur) bone. NOTUM inactivates WNTs by removing the essential palmitoleate required for activating Frizzled receptors. Notum KO mice had elevated bone mass and, aside from defects in dentin mineralization, no non-skeletal phenotypes. Elevated cortical bone thickness occurred throughout the skeleton, with trabecular bone unchanged. Treating male mice weekly with NOTUM neutralizing antibody 2.78.33a at doses from 0.3 to 10 mg/kg for 4 weeks increased midshaft femur cortical thickness from 3 to 10 %. Treating male mice with the orally active NOTUM inhibitor LP-922056 at 10 mg/kg for 4 weeks increased ($P < 0.001$) serum ALP (36 %), serum PINP (66 %), femoral neck BV/TV (5 %), LV5 vertebral body cortical shell BV/TV (9 %) and both cortical thickness (12 %) and strength (29 %) of the midshaft femur. Male mice treated with LP-922056 daily for 12 weeks at doses of 1, 3 or 10 mg/kg showed dose-dependent increases in cortical bone thickness of the humerus (5 to 15 %), femur (9 to 17 %) and rib (12 to 27 %). Male mice treated with LP-922056 twice weekly (Mondays and Thursdays) for 12 weeks at doses of 3, 10 or 30 mg/kg showed dose-dependent (4 to 11 %) increases in midshaft femur cortical thickness. Treating both intact and OVX female rats with LP-922056 at 30 mg/kg for 18 weeks increased ($P < 0.002$) cortical bone parameters in femur, tibia, humerus, radius, ulna, rib, femoral neck and vertebral body cortical shell. Treatment stimulated endocortical BFR (measured between 1 and 9 weeks) at the midshaft femur, distal tibia and rib. As a secreted enzyme inhibitable by neutralizing antibodies and orally active drugs, NOTUM is a potential drug target for stimulating modeling-dependent endocortical bone formation and treating osteoporosis.

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EFFICACY OF SHORT TERM TERIPARATIDE FOR UNTREATABLE HIP AND KNEE BONE MARROW EDEMA SYNDROMES

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The use of magnetic resonance (MRI) for the diagnosis of hip and knee pain revealed a set of conditions that occur with epiphyseal bone edema[1]. The so-called bone marrow edema syndromes[2] (BMEs) are challenging for clinicians because it includes a variety of diseases such as transient bone marrow edema and osteoporosis, complex regional pain syndrome I (CRPS type 1), stress fractures and bone bruise, subchondral insufficiency fracture and osteonecrosis. In most cases the medical history facilitate us the correct diagnosis but it is not always true and unfortunately is not always possible to identify a causative factor. The lack of knowledge on the pathological processes between this diseases and the demonstration that some of these can evolve into osteonecrosis, the theory that BMEs are a variable form of an early stage or self-limiting osteonecrosis, further complicates the diagnostic process and the formulation of a correct therapeutic strategy[3]. The goal of conservative treatment is to

control symptoms, prevent or delay surgery and to protect the joint. The conservative treatments commonly used are AINS, painkillers and opioids, bisphosphonates, iloprost and prostaglandins and hyperbaric therapy all to be combined with rehabilitation, physical therapies and partial or non weight bearing. Therapy with both sysadoas and hyaluronate is useful for secondary osteoarthritis. Despite these treatments have proven to be effective in most of the cases, it is still a subset of patients who are classified as untreatable and are generally intended for prosthetic surgery.

In this patients, the failure of the above mentioned therapy has led us to try a three months therapy with teriparatide when the maximum anabolic effect is present before promoting bone remodeling[4]. Moreover, the up regulation of growth factors like bFGF-2 and IGF-1[5], RANKL[6], the influence on the Wnt/β-catenin signaling pathway and the transcriptional suppression of the sclerostin[7] gene may play an important role on the regulating effect of teriparatide on bone. Teriparatide has also an adrenal effect increasing plasma and urinary cortisol lasting as long as therapy[8] probably regulating the inflammatory cascade. Lastly, teriparatide has proven to accelerate fracture healing and have a potential effect in increasing bone volume within joints and inhibiting articular cartilage degeneration[9,10]. Until now we have treated nine patients, six of which have exceeded 1 year of follow-up and one over two years. Of these seven patients, two of them with primary hip osteonecrosis, two with post traumatic knee osteonecrosis, two with CRPS type 1 of the knee and one with subchondral insufficiency fracture. Concomitant therapy was with sysadoas, intraarticular hyaluronate and analgesics as needed. All patients experienced a rapid response in terms of pain and progressive recovery of joint function. After three months, teriparatide was discontinued with the only indication to rehabilitation and chondroprotection. MRI at three months showed an almost complete resolution of the initial consensual to the clinical response. Three patients underwent control at 1 year which shows no progression.

We believe that teriparatide is considered as an alternative treatment to refractory BMEs, although further confirmation of efficacy is needed.

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CENTRAL ADIPOSITY HAS A DETRIMENTAL IMPACT ON TRABECULAR BONE IN OBESE POSTMENOPAUSAL WOMEN: A RETROSPECTIVE STUDY

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Objective: To evaluate the effect of visceral adipose tissue (VAT) on bone microarchitecture in postmenopausal obese women.

Materials and Methods: In this retrospective study we reported data from medical records of obese postmenopausal women (BMI ≥30 kg/m^2) referring to our outpatient rehabilitation service for the prevention and management of osteoporosis over a 3-year period. In these patients we measured BMD at lumbar spine (LS BMD) and at femoral neck (FN BMD), trabecular bone score (TBS), VAT volume and VAT mass. The population was divided into quartiles of VAT volume (VAT < 1.398 cm^3; VAT between 1.398 and 1.764 cm^3; VAT between 1.765 and 2.371 cm3; VAT > 2.371 cm^3). The differences between groups in terms of TBS, according to cutoff proposed by Silva et al. [1], were assessed using SPSS 21.0 to perform the Kruskal-Wallis test for independent samples.

Results: We analyzed data of 226 women (mean age 64.56 ± SD 8.42, mean BMI 34.18 ± SD 3.32). There were no statistically significant differences for age between groups ($p = 0.332$). In our population, higher VAT volume was associated with a significant worsening of the trabecular bone microarchitecture ($p = 0.003$). In particular, in the first quartile, 40.8 % of patients had a TBS ≤ 1.200, whereas in the higher quartile 72.2 % of women had degraded microarchitecture.

Conclusions: Nowadays, the relationship between adipose tissue and bone is not well understood. Moreover, the bone involvement in obese patients is still controversial. The amount of visceral adipose tissue (VAT) might be