Summer Issue, 2014

OSTEOS NEWSLETTER

Newsletter of the Lebanese Society for Osteoporosis and Metabolic Bone Disorders

Executive Board

President
Faysal El-Kak, MD

Founding President
Ghada El-Hajj Fuleihan,MD,MPH

Vice-President
Georges Halaby, MD

Treasurer
Jad Okais, MD

Executive Committee
Rafic Baddoura, MD, MPH
Ghada El-Hajj Fuleihan,MD,MPH
Jad Okais, MD
Muhieddine Seoud, MD
Assaad Taha, MD

Non Voting Members
Assaad Mohanna, MD
Walid Saghir, MD
Imad Uthman, MD

Layout & Design by
Sarine El Daouk

Welcome note

Dear colleagues,

It is our pleasure to welcome you to this issue of your newsletter.

In this issue we selected for you some highlights from the annual meeting of the American Society for Bone and Mineral Research that was held lately in Houston, Texas.

We would like to take the occasion to invite you to the 6th annual meeting of your society OSTEOS, that will be held early December of this year. We are confident that the meeting will offer many learning opportunities to all of us because of its rich program that covers wide spectrum of areas and of the highly qualified international and local faculty.

Enjoy reading the issue and see you in December!!

Editor-in-Chief: Asma Arabi, MD, MSc

Mission of OSTEOS

To enhance state-of-the-art knowledge and expert care for osteoporosis and other metabolic bone disorders in Lebanon through education, research and service.

To join OSTEOS please visit our website on: http://www.osteos.org.lb

For your suggestions, please contact us: osteos@osteos.org.lb

Bisphosphonate Drug Holiday and Fracture Risk

Adams et al compared the incidence of osteoporosis-related fragility fractures in patients who discontinued bisphosphonates (BPs) for at least 12 months (drug holiday) to those who continued to use BPs (persistent use) in a retrospective cohort study of 28620 women aged ≥45 years, with ≥3 years exposure to BPs, observed for 111997 person-years. Drug holiday was defined as ≥12 months with BP use at 0% adherence. Persistent use status required ongoing use at ≥50% adherence. Persistent users and drug holiday subjects were compared with regard to several demographic and clinical characteristics. The cohort of 28620 women included 17123 (59.8%) persistent BP users and 11497 (40.2%) drug holiday subjects.

The drug holiday group had fewer comorbidities, higher baseline T-scores, and lower fracture and fall risk scores. A total 3,571 osteoporosis-related fractures were observed. The unadjusted rate ratio (RR) for any osteoporosis-related fractures for drug holiday compared to persistent use was 0.87 (95% CI 0.81-0.94), but RR=1.0 (95% CI 0.9-1.2) for hip fractures only. The time-varying models suggested no differences in fracture risk (hazard ratio (HR) 0.90 (95% CI 0.80–1.00), after adjustment for baseline fall and fracture risk, comorbidities, and other bone-active medication use. Similarly, no difference in hip fracture risk was observed. The authors concluded that women who undertake a holiday from BP use are not at greater risk of osteoporosis-related fragility fractures, nor hip fractures specifically, than are women who continue to use BPs persistently.

Annette Adams et al: Presentation 1045.

Skeletal Effects of PTH in Combination with Denosumab or Alendronate

Tsai et al aimed to better define the pro-resorptive properties of teriparatide (TPTD) in the absence or presence of an antiresorptive drug. 18 postmenopausal osteoporotic women (52 -81 years) were randomized to 2 treatment groups. Bone markers were measured at baseline both immediately prior to and 4-hours after a single 8 AM 40-mcg SC TPTD injection. When the 4-hour sampling was complete, subjects in group 1 received DMAB 60 mg SC and subjects in group 2 started oral weekly alendronate (ALN) 70 mg. 8-weeks later, CTX, P1NP, and OC were again measured immediately before and 4-hours after a TPTD 40-mcg injection.

At baseline, TPTD induced a significant and similar increase in mean CTX in both treatment groups (ALN 47±13%, DMAB 49±17%). After 8 weeks of antiresorptive therapy, TPTD maintained its ability to increase CTX (44±34%) in the ALN group but not in the DMAB group.

In summary: 8 weeks of DMAB, but not ALN, fully inhibits the high-dose TPTD–induced increase in CTX. These results suggest that combining DMAB with higher doses of TPTD may be an effective osteoporosis treatment strategy.

Joy Tsai et al, Plenary Sessions, ASBMR 2014, Presentation FR0377.

The Transition from Denosumab to Teriparatide or from Teriparatide to Denosumab

The DATA study assessed the effects of 2-years of denosumab (DMAB 60-mg every 6-months), teriparatide (TPTD 20-µg daily), or both, in postmenopausal osteoporotic women. In DATA-Switch, women who received DMAB for the first 2-years were switched to TPTD and those who received either TPTD or TPTD+DMAB were switched to DMAB alone. BMD was measured 6 and 12 months after switching treatments. In women switched from TPTD to DMAB (n=27), 12-months of DMAB increased BMD by an additional 5.7% at the spine, 3.5% at the femoral neck (FN), and 3.1% at the total hip (TH), resulting in net 3-year BMD increases of 15.1% at the spine, 5.7% at the FN, and 5.3% at the TH. Switch from DMAB to TPTD (n=24), resulted in a net 3-year change in BMD of 10.4% at the spine, 1.6% at the FN and 0.7% at the TH. Switching from combination therapy to DMAB alone (n=21) resulted in net 3-year increases of 15.0% at the spine, 7.2% at the FN, and 7.1% at the TH.

After a total of 3-years of therapy, the increase in TH BMD remained greater in women who received combination therapy followed by DMAB than in either other groups (P=0.04). The investigators concluded that DMAB prevents bone loss and increases BMD in women treated with TPTD. TPTD, however, does not fully prevent the bone loss that occurs after DMAB discontinuation, particularly at the hip. Thus, the use of TPTD immediately after DMAB may not be advisable, especially in women at very high fracture risk. Two years of combined TPTD and DMAB followed by DMAB alone results in the most favorable effects on hip BMD and may be a useful treatment approach in high-risk patients.

Benjamen Leder et al, ASBMR 2014, Presentation 1150.

Romosozumab Followed by 1 Year of Denosumab or Placebo in Postmenopausal Women

One year treatment with the sclerostin antibody romosozumab (Romo) was associated with increased bone mineral density (BMD) and bone formation and with decreased bone resorption in postmenopausal women with low BMD. In this study, McClung et al reported the results of 2 years phase 2 study of treatment with Romo followed by 1 year of denosumab (DMAb) or placebo in 419 postmenopausal women age 55- 85 years with a lumbar spine (LS), total hip (TH), or femoral neck (FN) T-score ≤ –2.0 and ≥–3.5. Women received 1 of 5 regimens of Romo (70 mg QM, 140 mg QM, 210 mg QM, 140 mg Q3M, 210 mg Q3M; or placebo for 2 years. At the end of 2 years, eligible subjects entered a 1-year extension phase and were re-randomized 1:1 within their original treatment group to placebo or DMAb 60 mg Q6M.

Romo led to rapid and marked increases in LS & TH BMD during year 1 and continued increases through year 2. The largest gains were observed with Romo 210 mg QM, with BMD increases of 15.7% (LS) and 6.0% (TH). Women receiving Romo 210 mg QM who transitioned to DMAb continued to accrue BMD at a rate similar to that in the second year of Romo; in those who transitioned to placebo, BMD returned towards pretreatment levels. Romo induced rapid stimulation of bone formation (P1NP) and decreased bone resorption (CTX). Increases of P1NP were transitory, returning towards baseline within 6 to 12 months and remaining below baseline through year 2. CTX remained below baseline through year 2. In subjects receiving Romo 210 mg QM who transitioned to DMAb: P1NP and CTX decreased; for those who transitioned to placebo: P1NP gradually returned to pretreatment levels, while CTX initially increased above baseline and gradually returned towards baseline. In conclusion, Romo led to rapid and marked increases in lumbar spine and total hip BMD over 2 years, which continued with DMAb and resolved after transition to placebo.

McClung et al, ASBMR 2014,

Atypical femoral fractures: Sensitivity and specificity of radiographic characteristics

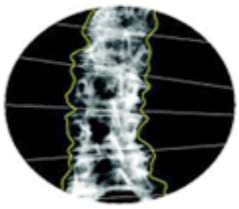
To understand the real-world application of the 2013 ASBMR atypical femoral fracture (AFF) criteria, Admas et al assessed the sensitivity and specificity of radiographic features for distinguishing AFF from other subtrochanteric or diaphyseal fractures among women enrolled in a large integrated health care organization. The investigators identified 55 physician-validated AFFs and a sample of 39 non-AFF (nAFF). X rays reviewed by 4 independent osteoporosis experts. Using a standardized data collection tool based on the 2013 revised AFF case definition, reviewers indicated the presence or absence of the following characteristics viewable on radiograph: fracture location, fracture pattern, non-comminution, periosteal and/or endosteal, and cortical thickening. Sensitivity and specificity for each characteristic was calculated for each reviewer, and summarized across reviewers with the mean and range. The most highly sensitive factors for distinguishing between AFF and nAFF were subtrochanteric/diaphyseal fracture location (mean 99.4%, range 97.7-100%), lateral cortex transverse fracture pattern (mean 95.3%, range 90.2-97.7%), medial cortex transverse or oblique fracture pattern (mean 94.0%, range 83.3-100%), and minimal or non-comminution (mean 94.2%, range 88.6-97.7%). Of these factors, specificity was greatest for lateral cortex transverse fracture pattern (mean 72.8%, range 69.6-76.0%), while medial cortex transverse or oblique pattern was least specific (mean 11.2%, range 0-42.6%). Localized endosteal/periosteal reaction and generalized increase in cortical thickness were only moderately sensitive and specific.

Annette Adams et al, ASBMR 2014, Presentation FR0317.

Risedronate and Bone strength in postmenopausal women on aromatase inhibitors

Risedronate has been proven to prevent aromatase inhibitor-induced bone loss assessed by DXA. Lee et al analyzed the changes in volumetric bone mineral density (vBMD) and cortical geometry parameters at the proximal femur using QCT, in response to risedronate therapy, in a cohort of breast cancer patients on aromatase inhibitors. Women were classified according to risedronate administration: treated group (RIS, n=26) and control group (n=24). All patients had been taking AIs and calcium carbonate 1250 mg plus 1000 IU as cholecalciferol. BMD of neck (FN), trochanter, intertrochanter, and total hip (TH) and cortical geometry parameters were analyzed. The mean age of the patients was 58.1 ± 4.7 years. The mean duration of risedronate therapy was 633 days. QCT data were obtained at baseline and at 2 years. Risedronate blunted the decrease in vBMD: The mean 2-year percent change from baseline in total vBMD was -0.98% in RIS vs. -5.9% in control at the FN, +1.47% in RIS vs. -2.3% in control at the trochanter, +0.1% in RIS vs. -1.9% in control at the intertrochanteric region, and +0.77% in RIS vs. -2.8% in control at the TH ($p< 0.01$ for all comparisons). RIS treatment also significantly increased cortical thickness of the total hip +0.3% vs. –8.1% in control group ($p=0.007$) and decreased cortical buckling ratio compared to the control group at neck, trochanter and total hip. The investigators concluded that this study showed preventive effects of oral risedronate on bone geometry as well as volumetric bone mineral density at the proximal femur in postmenopausal women with breast cancer taking AIs.

DENSITOMETRY CORNER



Effect of Vertebral Artifact and Exclusions on Fracture Prediction from Lumbar Spine BMD and TBS (Trabecular Bone Score): The Manitoba BMD Cohort

Background: Age-related spondylosis is common and degrades lumbar spine DXA scan quality. Spine TBS (trabecular bone score) may be less sensitive to spondylosis but has not been studied in relation to fracture outcomes.

Methods: Using a registry of all clinical DXA results for Manitoba, Canada, Leslie et al identified women age >40y with baseline spine DXA (GE Prodigy) from years 1999-2011. Vertebral exclusions were identified by ISCD-certified physicians at the time of initial clinical reporting. Spine TBS was measured by researchers at the University of Lausanne blinded to clinical outcomes. BMD and TBS T-scores were derived for the total spine, individual vertebral levels, minimum/maximum, and (if there were vertebral exclusions) the non-excluded and excluded levels. Incident major osteoporotic fractures (MOFs) and clinical vertebral fractures (VFs) were identified from population-based health services data, and fracture discrimination estimated from area under the ROC curve (AUROC).

Results: 47,736 women met the inclusion criteria. 15,938 (33%) had vertebral exclusions and these varied by level: L4 98%, L3 63%, L2 14%, L1 10%. Vertebral exclusions had a large effect on the BMD T-score (non-excluded levels -1.6, excluded levels -0.4) and on the TBS T-score (non-excluded levels -1.4, excluded levels -0.5). AUROC for predicting MOF from total spine BMD T-score was 0.673 in women without vs 0.642 with vertebral exclusions; non-excluded levels had higher AUROC (change +0.016) but excluded levels had worse AUROC (change -0.007). AUROC for MOF from total spine TBS T-score was 0.644 in women without vs 0.613 with vertebral exclusions; non-excluded levels had higher AUROC (change +0.010) but excluded levels had worse AUROC (change -0.037).
Similar results were seen for clinical VFs based upon BMD (AUROC change non-excluded levels +0.026, excluded levels -0.011) and TBS (AUROC change non-excluded levels +0.019, excluded levels -0.055). In women with vertebral exclusions, BMD or TBS T-score for L1 showed higher AUROC for MOF prediction than for any other vertebral level, and minimum T-score showed better MOF prediction than maximum T-score.

Summary: Spine DXA artifacts requiring vertebral exclusions affect both spine BMD and TBS. Excluded levels had higher BMD and TBS and worse fracture prediction. Exclusion of levels affected by artifact improved fracture prediction. BMD reporting procedures excluding lumbar spine artifacts also appear to be applicable to TBS.

William Leslie et al, ASBMR 2014, Presentation 1065

Mark your calendar

Nov 14-16, 2014	IOF Regionals 5th Asia-Pacific Osteoporosis Meeting	Taipei, Chinese Taipei
Dec 5-6, 2014	6th annual meeting of the OSTEOS	Movenpick Hotel, Beirut
Dec 7-9, 2014	27e congrès français de Rhumatologie	CNIT-La Defense, Paris-France
Jan 18, 2015	XXVIIIème Journée scientifique du GRIO - Janvier 2015	Paris-France
Mar 26 -29, 2015	WCO-IOF-ESCEO World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases	MiCo - Milano Congressi, Milan-Italy
May 25-28, 2015	4th Joint Meeting of ECTS and IBMS	Rotterdam, The Netherlands
Dec 5-7, 2015	IOF Regionals 3rd Middle East and Africa Osteoporosis Meeting	Abu Dhabi, United Arab Emirates