

**SUN-396**

Despite clinical strides in the treatment of osteoporosis in several diverse medical conditions, the ability to maintain bone has proven to be exceedingly difficult in individuals with severe immobilization. Fifty to 60% of bone mineral density (BMD) at the epiphyseal and metaphyseal regions of the long-bones of the lower extremities may be lost over the first couple of years after spinal cord injury (SCI). Once a large amount of bone has been lost, it would be challenging to restore BMD, trabecular architectural integrity, and mechanical strength to provide protection against long-bone fractures of the lower extremities. Persons with neurologically complete forms of SCI have marked loss of BMD of the lower extremities, predisposing to fracture, especially at the knee. Denosumab, a commercially available human monoclonal antibody of the IgG<sub>2</sub> immunoglobulin isotype with a high affinity and specificity for binding RANKL to antagonize its action, may provide an immunopharmacological solution to the rapid progressive deterioration of sublesional bone after SCI. Twenty-six patients with motor-complete SCI [International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) grade A and B] were randomized to receive denosumab or placebo at baseline (BL), 6, and 12 months. Ten participants in the denosumab group and 8 participants in the placebo group completed the 18-month clinical trial [ClinicalTrials.gov (NCT01983475)]. Dual energy x-ray absorptiometry (DXA; Lunar Prodigy Advance, all software version 12.20.023; EnCORE, GE Medical Systems, Madison, WI) and peripheral quantitative computed tomography (pQCT; Stratec XCT 3000; STIM designs, Carmel, CA) imaging were performed. Within group paired analysis revealed a significant decrease for areal BMD (aBMD) from BL in the placebo group that started at month 3 for the distal femoral epiphysis (DFE), distal femoral metaphysis (DFM), and total hip (TH) and at month 6 for the femoral neck (FN), and at month 12 for the proximal tibial epiphysis (PTE); the loss in aBMD progressed to 18 months for all the skeletal regions of interest (ROI). At 18 months, the percent change at the ROI for the denosumab vs. placebo groups were: DFE (1.1% ± 7.5 vs. -30.0% ± 11.9, respectively, p<0.001 and p<0.001), DFM (1.2% ± 6.4 vs. -17.2% ± 14.2, p<0.01), TH (3.3% ± 8.7 vs. -25.6% ± 7.6, p < 0.001), and PTE (-1.7% ± 8.2 vs. -24.1% ± 12.3, p<0.001). At 18 months, pQCT at the 4% tibial region confirmed the DXA findings at proximal tibial; at the 38% tibial region, a trend toward loss of total volumetric BMD (vBMD) was observed (-0.7% ± 4.5 vs. -16.9% ± 20.0, p<0.09), but cortical vBMD was similar between the denosumab and placebo groups, suggesting trabecular loss at the tibial shaft. In summary, the findings suggest that denosumab, if treatment is initiated within 3 months of acute SCI, appears to be an efficacious approach to maintain BMD at the knee and hip regions.

## Diabetes Mellitus and Glucose Metabolism

### CLINICAL STUDIES IN OBESITY, DIABETES RISK, AND CARDIOVASCULAR OUTCOMES

#### *Nattokinase to Improve Insulin Sensitivity and Weight Loss in Women with Obesity +/- Diabetes*

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**SAT-618**

Background: Diabetes (DM) and obesity are related health issues which are increasing in prevalence. But not all obesity is related to DM. Women suffering from Lipedema are categorized as gynoid obese. Nattokinase (Natto) is an enzyme supplement that has been shown to degrade fibrin. Patients with obesity tend to have elevated clotting factors which can lead to adipose tissue hypoxia, impaired insulin signaling, and lead to insulin resistance. Research in fat disorders noted that fat biopsies from women with Lipedema likely had micro-clots, and patients with Lipedema treated with Natto reported a decrease in clothing size and fat distribution. Objective: Determine the effect of Natto on participants with Obesity and DM and in patients with Lipedema without DM. Materials and Methods: Group 1: Involved subjects with Obesity and DM. This was a double blinded, randomized controlled clinical trial over 3 months. A total of 17 female patients were recruited from a rural clinic. Nine received Natto 2,000 FU daily and eight received an identical placebo capsule daily. Fasting labs, questionnaires, bioimpedance, and anthropometric measurements were completed at Baseline and 3 months. Group 2: 42 women with Lipedema seen at a Fat Disorder Clinic. 21 received Natto and 21 did not. We compared for weight only from the day Nattokinase was started until follow-up, which varied from 4 months to 1 year 8 months. Results: Group 1: After 3 months, there was no difference in weight loss in both groups. Per Bioimpedance, more subjects lost water weight in the Natto group (63%) compared to Placebo (33%). More subjects in the Natto group had a decrease in HbA1c (43%) compared to Placebo (22%), with average decrease in the Natto group of 0.9%. Also, more subjects in the Natto group had lower fasting insulin levels (75% vs 22%), lower fasting glucose level (50% vs 22%) and lower HOMA index (63% vs 22%). Group 2: 57% of patients in the Natto group lost weight compared to only 33% of patients not on Natto. Conclusions: In participants with obesity and DM, regardless of weight loss, metabolic health improved after taking Natto for 3 months. Higher percentage of subjects in the treated group had improved HbA1c, fasting Insulin, glucose, and HOMA score. We hypothesize that if treatment time was beyond 3 months, further metabolic improvement would be noted, indicating that Natto could have potential as an adjunct to DM care. The difference in weight loss between Metabolic Obesity and Lipedema reflects the difference in adipose tissue, likely differing in etiology and pathophysiology. Further studies are needed to evaluate long term benefits of Natto, including larger and longer randomized controlled trials, and assessment of clotting factors.

## Bone and Mineral Metabolism

### BONE AND MINERAL CASE REPORTS I

#### *Out of Sight, out of Mind: PHEX 3'-UTR C.\*231A>G X-Linked Hypophosphatemia in Adults: A Case Study of One Family Pedigree with a Widely Variable Phenotype*

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