

Effects of Denosumab on Bone Mineral Density, Markers of Bone Metabolism and Bone Microarchitecture in Women with Anorexia Nervosa: A Pilot Study

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VI. Biostatistical Analysis

Sample Size and Justification: Group sample sizes of 20 (active therapy) to 10 (placebo) for a total N=30 will achieve 87% power to reject the null hypothesis of equal means when the population mean difference is 4.5 with a standard deviation of both groups of 3.4 and with a significance level of (alpha) of 0.050 using a 2-sided 2-sample equal-variance t-test. This is based on the difference in percent change in spine bone density between the denosumab and placebo groups in [REDACTED].

Data Analysis Plan:

The data analysis plan for the main study and the substudy will be as follows: Variables will be tested for normality using the Shapiro-Wilk test, and if non-normal, variables will be log-transformed before analysis. Mean percent change from baseline in bone mineral density, HRpQCT variables and markers of bone metabolism will be analyzed using analysis of covariance, with treatment as the main effect, and baseline value as a covariate. For the substudy, a secondary analysis will be performed to determine whether gains achieved in the denosumab group are maintained through the subsequent 12-month study period using a repeated measures within group model.

Main Study Endpoints:

Primary:

Percent change from baseline in lumbar spine bone mineral density by dual energy xray absorptiometry (DXA) at 12 months.

Secondary:

Percent change from baseline in bone mineral density of hip (total and femoral neck) and radius by DXA at 12 months.

Percent change from baseline in markers of bone metabolism: CTx, P1NP, Osteocalcin over 12 months.

Exploratory:

Percent change from baseline in HRpQCT of the tibia and radius variables: trabecular thickness and spacing; cortical thickness and porosity; percent change from baseline in ITS variables; percent change from baseline in finite element analysis modeling of bone strength

Substudy Endpoints:

Primary:

Lumbar spine BMD at 24 months.

Exploratory:

Radial and tibial HRpQCT variables at 24 months: trabecular thickness and spacing; cortical thickness and porosity; percent change from baseline in ITS variables; percent change from baseline in finite element analysis modeling of bone strength

Markers of bone metabolism at 24 months: CTx, P1NP, Osteocalcin.