Population PK/PD Modeling of Lumbar Spine Bone Mineral Density Response to 12 Months of Treatment with the Cathepsin K Inhibitor, Odanacatib, and Simulations to Further Evaluate the Dose-Response Relationship

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Background and Objectives

- The relationship between lumbar spine BMD (%) change from baseline and %CFD (LSMD) was evaluated using the Lumbar Spine BMD study, a prospective, randomized, placebo-controlled trial (study 76-203). The BMD (LSMD) model consisted of times from randomization to lumbar spine BMD at baseline, treatment, and study day.
- The impact of the subject's body composition and bone turnover parameters on AUC (time) was evaluated using the lumbar spine BMD model.
- The relationship between lumbar spine BMD (%) change from baseline and %CFD (LSMD) was evaluated using the Lumbar Spine BMD study, a prospective, randomized, placebo-controlled trial (study 76-203). The BMD (LSMD) model consisted of times from randomization to lumbar spine BMD at baseline, treatment, and study day.

Overview of Study Design

- A Phase II dose-ranging study in 399 women with osteoporosis is ongoing to potentially account for differences in the drug lot used in differing study
- The Impact of the subject's body composition and bone turnover parameters on AUC (time) was evaluated using the lumbar spine BMD model.
- The relationship between individual lumbar spine BMD (%) change from baseline and %CFD (LSMD) was evaluated using the Lumbar Spine BMD study, a prospective, randomized, placebo-controlled trial (study 76-203). The BMD (LSMD) model consisted of times from randomization to lumbar spine BMD at baseline, treatment, and study day.

Results

- The PK model was developed in NONMEM using data from 200 women randomized to placebo, 60 mg, 25 mg, 50 mg, and 100 mg doses of odanacatib. The PK model was developed using a one-compartment model with linear absorption and elimination rate constant terms. The baseline term and a placebo effect were incorporated.
- The relationship between lumbar spine BMD (%) change from baseline and %CFD (LSMD) was evaluated using the Lumbar Spine BMD study, a prospective, randomized, placebo-controlled trial (study 76-203). The BMD (LSMD) model consisted of times from randomization to lumbar spine BMD at baseline, treatment, and study day.

Discussion

- The relationship between lumbar spine BMD (%) change from baseline and %CFD (LSMD) was evaluated using the Lumbar Spine BMD study, a prospective, randomized, placebo-controlled trial (study 76-203). The BMD (LSMD) model consisted of times from randomization to lumbar spine BMD at baseline, treatment, and study day.
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Conclusions

- The relationship between lumbar spine BMD (%) change from baseline and %CFD (LSMD) was evaluated using the Lumbar Spine BMD study, a prospective, randomized, placebo-controlled trial (study 76-203). The BMD (LSMD) model consisted of times from randomization to lumbar spine BMD at baseline, treatment, and study day.
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