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TITLE: Prevention of Bone Loss after Acute SCI by Zoledronic Acid: Durability, Effect on Bone Strength, and Use of Biomarkers to Guide Therapy

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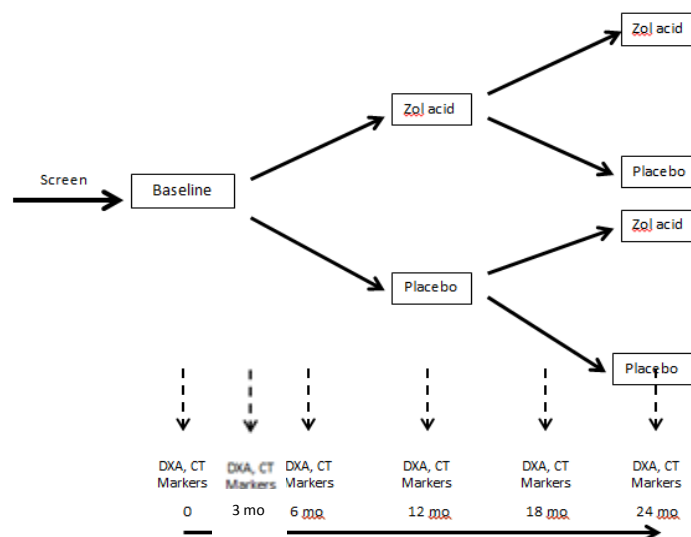
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14. ABSTRACT Rapid bone loss is a universal accompaniment of acute spinal cord injury (SCI) and leads to severe loss of bone mass and bone strength with a marked increased risk of fracture. This 24 month double-blind, randomized, placebo-controlled study evaluates in 60 participants the efficacy (bone mass and bone strength) and safety of zoledronic acid administered early after acute SCI to prevent bone loss, the duration of its effects and the value of using biomarkers to guide therapy. Data collection (bone imaging and biomarkers) occurs at baseline and after 3, 6 and 12 months during the first year; participants are re-randomized after 12 months with subsequent data collection at 18 and 24 months. Currently, all regulatory requirements for the study have been completed. Thirty (30) participants have been randomized and treated. No unexpected safety events have occurred. Data collection is on-going and additional patients are being screened for study entry.					
15. SUBJECT TERMS Spinal cord injury, bone mass, bone strength, osteoporosis, zoledronic acid					
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INTRODUCTION:

Rapid bone loss is a universal accompaniment of acute spinal cord injury (SCI) and leads to severe loss of bone mass and bone strength with a marked increased risk of fracture. The study proposed is a 2 year, randomized, double-blind placebo-controlled study of zoledronic acid to evaluate its efficacy and safety for the prevention of bone loss and maintenance of bone strength in individuals with recent onset SCI (see diagram below). At the end of the first year of the study, each treatment groups will be re-randomized to either zoledronic acid or placebo to evaluate the durability of response to zoledronic acid and the utility of serum bone markers to guide therapeutic decision making. DXA imaging, CT imaging and bone markers will be obtained at baseline, 3 months, 6 months, 12 months, 18 months and 24 months.



KEYWORDS: spinal cord injury, bone mass, bone strength, osteoporosis, zoledronic acid

OVERALL PROJECT SUMMARY:

All objectives outlined in the Statement of Work to be completed during the second year have been completed. All regulatory approvals have been maintained. Screening, enrollment and treatment of participants (Specific Aim 1, Major Task 3) continues, with 30 participants currently randomized and active in the study. Data are being obtained and entered into the study database, and study materials are being collected and maintained for future assay (biomarkers; part of Specific Aim 2, Major Task 1) or for image analysis (CT bone scans; part of Specific Aim 3, Major Task 1). As the investigators remain blinded to allocation of treatment assignment, it is not possible to know efficacy results until the end of the study. Safety is being continually monitored by collection of adverse events and their evaluation at a regularly held data safety monitoring committee meetings. Regular meetings with the medical monitor continue for review of all AEs and study procedures. No safety concerns have been identified and no changes in the study proposed.

Recruitment has been largely on track after a slightly delayed start due to delay from what was anticipated of regulatory approvals. There have been no impediments and treatment and data collection are proceeding without issues. No changes have been made in the statement of work and

only minor modifications of the protocol and informed consent have been made to align with the updated package insert (April 2016) for the study drug.

KEY RESEARCH ACCOMPLISHMENTS:

There are no outcome data available to date. As this is a blinded clinical trial, scientific data relating to study objectives will not be available until all participants have concluded the study, data cleaned and data base locked, and analyses completed.

CONCLUSION:

This project has not progressed to the point of being able to provide any conclusions in regard to the effect of these specific interventions on bone mass or bone quality in people after spinal cord injury. If benefit is shown, this intervention has the potential to reduce fracture incidence in people experiencing acute SCI.

PUBLICATIONS, ABSTRACTS AND PRESENTATIONS:

None.

INVENTIONS, PATENTS AND LICENSES:

None.

REPORTABLE OUTCOMES:

None.

OTHER ACHIEVEMENTS:

None.

REFERENCES:

None.

APPENDICES:

None.

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Prevent Bone Loss
to Prevent Fractures

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