
Abbreviated Clinical Study Report: BMTI-2006-03-EU

Title Page

Study Title: A Human Clinical Trial to Evaluate the Safety and Clinical Utility of *GEM OSI*™ as a Bone Regeneration System in Foot and Ankle Arthrodesis Procedures

Study Number: BMTI-2006-03-EU

Study Phase: Phase II study

Study Design: Prospective, open label, multi-center trial

Product Name: *Augment*™ Bone Graft (*Augment*; previously called *GEM OSI*™)

Formulation: Two components: Package of β -tricalcium phosphate with rhPDGF-BB (becaplermin) solution

Indication: Bone regeneration in foot and ankle fusions

Study Initiated (first subject enrolled): May 21, 2007

Clinical Study Report (last subject completed 24 weeks): March 11, 2010

Principal Investigators: Multicenter (see Appendix 15.1.4)

Sponsor: BioMimetic Therapeutics, Inc.
389 Nichol Mill Lane
Franklin, TN 37067
Telephone: 615-844-1280

Responsible Medical Officer: Dr. Michel Levy
56, Quai Alphonse le Gallo
92513 BOULOGNE-BILLANCOURT Cedex
FRANCE

Final Date: Version 1.1 – January 2011

Confidentiality Statement

This clinical study report contains proprietary information from BioMimetic Therapeutics, Inc. Please consider accordingly that the information shall not be disclosed to any third party without prior consent of the Sponsor, BioMimetic Therapeutics, Inc.

Synopsis

Sponsor:

BioMimetic Therapeutics, Inc.

Name of Finished Product:

Augment Bone Graft

Name of Active Ingredient:

Two components: Package of
 β -TCP with rhPDGF-BB
(becaplermin) solution

Study Title:

A Human Clinical Trial to Evaluate the Safety and Clinical Utility of *GEM OSI™* as a Bone Regeneration System in Foot and Ankle Arthrodesis Procedures

Investigators and Study Centers:

Multicenter (see Appendix 15.1.4)

Publication (reference): None

Studied Period:

May 21, 2007 – March 11, 2010

Phase of Development:

Phase II

Objectives:

The study objective is to evaluate the safety and clinical utility of a synthetic bone regeneration system (*Augment Bone Graft*) in a representative clinical model (foot and ankle fusions).

Methodology:

This prospective, open-label, multi-center clinical trial was undertaken to evaluate the safety and clinical utility of a synthetic bone regeneration system (*Augment Bone Graft*) in a representative clinical model (foot and ankle fusions).

The study intent was to enroll up to 125 subjects requiring fusion in the midfoot, hindfoot or ankle (tibiotalar) requiring the use of bone graft.

Each subject was to have a physical exam of the anatomical region to be treated incorporating medical history and injury/disease etiology. The subjects underwent a foot/ankle fusion procedure using open surgical technique with a synthetic bone regeneration system (*Augment Bone Graft*).

The fusion constructs required adequate reduction and stabilization with rigid fixation intra-operatively in order to meet final study eligibility. Subjects were immobilized according to standardized operative and post-operative protocols.

The investigators, who were fellowship-trained and board-certified foot and ankle surgeons,

performed clinical and radiographic assessments (as required by protocol) to monitor healing/union status. A masked independent radiographic assessment was performed by a designated fellowship-trained and board-certified musculoskeletal radiologist who assessed radiographic parameters for fusion.

All enrolled subjects were to be monitored over a nine-month period to evaluate for clinical and safety outcomes, including incidence of loss of reduction, infection, non-union, need for revision fusion surgery, and associated complications with hindfoot and ankle fusion procedures, in addition to the occurrence of other adverse effects.

A protocol amendment has been made in Final Revision 2, (03 December 2008) on:

- Omission of Visit 9 (24-month follow-up visit) and
- Completion of enrollment

During the course of the study, routine monitoring revealed deficiencies in study compliance, which noted a considerable number of missing radiographic images, having not been taken or misplaced by the primary investigator.

As this study is an uncontrolled study, the incomplete primary efficacy data has led the sponsor to present an abbreviated clinical study report including all safety data as outlined by ICH and other specific safety-related endpoints.

Number of Subjects (planned and analyzed):

Planned: 125

Analyzed: 108

Diagnosis and Main Criteria for Inclusion:

Male and female subjects over the age of 18 years of age requiring a hindfoot/ankle fusion procedure involving a bone grafting procedure.

Test Therapy:

Standard rigid fixation + *Augment Bone Graft*, containing β -TCP and 0.3 mg/mL rhPDGF-BB in sodium acetate buffer

Reference Therapy by History Comparison:

Standard rigid fixation + autologous bone graft (autograft)

Duration of Follow-up:

36 weeks (primary endpoint at 24 weeks)

Criteria for Evaluation:

Safety:

The analysis of safety-related data include frequency, severity, and relationship to investigational product for all adverse events; surgical site, drug, and infection complications associated with injury or standard surgical treatment, including non-union; system organ class (SOC) classification of adverse events by treatment group; serious adverse events with narratives, subjects who discontinued the study due to death or other significant adverse events; and serum sample analysis for presence of anti-rhPDGF-BB antibodies.

Statistical Methods:

Data were summarized descriptively only. No inference procedures were performed and no comparison was made to historical control.

Summary of Results

Disposition of Subjects :

Out of 130 screened subjects, 108 subjects are represented in the safety population.

Safety: There were 132 adverse events reported during the course of this study. Of all evaluable subjects, 64% (69) experienced at least one adverse event, with most subjects (62%; 67) experiencing the event after the surgery date. Five events of surgical wound infections were reported across five (5) subjects or 4.6%. There was only one (0.9%) surgical wound infection that was also categorized as a drug complication by the independent medical monitor. An adverse event was recorded for this subject as being an infection at the entrance site of the screw.

Twenty-five (25) serious adverse events were reported for this study with none related to investigational product. Additional information, including complete narratives, is found in Appendix 9.

Safety was also evaluated by radiography and CT scan review based upon available and assessable images as follows:

- At Week 36, 1% of joints showed evidence of abnormal bone formation at the fusion site, which was classified as excess callus formation.
- Graft fill in space may have decreased over time.
- The presence of β -TCP particles within soft tissue may have decreased over time.

For clinical and functional assessments, a general pattern of decline after surgery followed by improvement up to Week 36 was seen for pain, warmth and swelling at fusion site, weight-bearing status, and healing status. For other endpoints, there were varied responses. For range of motion, there was some improvement up to Week 36 for some subjects; however, the percentage of subjects reporting severe limitations at screening remained relatively constant through Week 36. A large majority of subjects (>90%) reported no evidence of infection and intact neurovascular status at all visits. For stability of fusion site, starting at Week 6 and consistently through Week 36, approximately 20% of subjects reported motion, and approximately 80% reported no motion at the fusion site.

Conclusions:

Safety: *Augment Bone Graft* was shown to be safe in this clinical trial involving 108 subjects studied for up to nine months.

Consistent with the extensive biocompatibility profile on the combination product and the historical safe use of each individual component, the study revealed no evidence of either

local or systemic adverse effects. There were no adverse outcomes attributable to the investigational product and the investigational product was found to be safe. Further, it is clinically important to surgeons and subjects that, with use of *Augment Bone Graft*, there was no morbidity associated with bone graft harvest.

Final Report Date: Version 1.1 – January 2011

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