Prefix (B2A-coated Ceramic Granules) for Lumbar Spinal Fusion: Preclinical and Preliminary Clinical Results

Brent L. Atkinson,1 Peter Jarzem,2 Khalid A. Sethi,3 Saeed A. Bajwa,3 Alejandro Reyes-Sanchez,4 Warren D. Yu,5 Joseph R. O’Brien5
batkinson@biosetinc.com

1BioSurface Engineering Technology (BioSET), Rockville, MD, USA, 2Montreal, Quebec, Canada, 3Johnson City, NY, USA, 4Mexico City, Mexico, 5George Washington University, Washington DC, USA

Introduction

Synthetic osteoconductive ceramics are by themselves insufficient as grafts to facilitate spinal fusion, a treatment for chronic back pain. Prefix is a new scaffold drug delivery system composed of ceramic granules coated with the bioactive peptide B2ATM and is in development to increase spinal fusion rates without the need for autologous iliac crest bone (ICB), the gold standard. B2A is a synthetic, receptor-targeted peptide that synergistically amplifies the biological response of BMP-2 and induces proliferation and migration of stem cells. The objective of these studies was to evaluate safety and effectiveness of Prefix in comparison to ICB in preclinical and clinical studies.

Materials and Methods

Prefix preparation. Prefix was prepared from vials of lyophilized peptide and porous, ceramic granules (80% TCP / 20% HA; Biomatante). The peptide is dissolved in water and added to the granules to which it binds. Once Prefix is implanted, the peptide is slowly released to the local environment.

Preclinical studies. Prefix with B2A (50-300 µg B2A/cc, n=10) mixed with ICB was evaluated in a rabbit posterolateral fusion (PLF) model. ICB was used as a positive control and uncoated granules with ICB was used as a negative control. Fusion was assessed at 6 weeks by radiography and palpation, and confirmed by histology and CT. Prefix with B2A (50-600 µg B2A/cc, n=8) plus ICB was compared to uncoated granules plus ICB in a sheep model of instrumented interbody spinal fusion and results evaluated after 4 months by CT and quantitative histomorphometry.

Clinical studies. International multi-center, prospective, randomized pilot studies were initiated to evaluate safety and preliminary effectiveness of Prefix/B2A plus local bone as compared to ICB in subjects with degenerative disc disease. Patients undergo transforaminal lumbar interbody fusion in concert with a posterior fixation and a cage.

Results

Preclinical studies. In the rabbit PLF model, treatment with Prefix/B2A resulted in significantly (p<0.05) higher incidence of fusion as compared to controls. In the sheep interbody fusion model, all Prefix/B2A doses had higher fusion rates as compared with the negative control. Histologically, bridging bone and new bone was observed in granule pores and between granules. No untoward events were attributed to B2A in either animal model.

Clinical studies. After 6 months, dynamic x-rays and CT for the first 8 patients demonstrated comparable spinal fusion rates for each group. Patient questionnaires from 12 patients at 3 months demonstrated that VAS scores for low back and leg pain decreased by >35mm and the Oswestry Disability Index improved by >22 points for each group compared to baseline. Preliminary safety data demonstrate the absence of serious device-related adverse events, radiolucency, ectopic bone or radiculopathy.

Discussion and Conclusions

There is a clinical need for in situ regenerative treatments that can consistently and safely increase fusion rates and eliminate the use of iliac crest autograft with its high complication rates. Prefix/B2A may provide a safe, less expensive and more effective alternative to current bone grafting materials and be a reliable alternative compared to iliac crest autograft.

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