AGA111, a Recombinant Human Bone Morphogenetic Protein 6 (rhBMP6), Improved Lumbar Interbody Fusion Success Following Single-Level Transforaminal Lumbar Interbody Fusion (TLIF) Surgery in a Phase I/II, Double-Blind, Placebo-Controlled, Randomized Study

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INTRODUCTION: AGA111 is a rhBMP6 that is mixed with autologous blood coagulum (ABC) for use in spinal fusion procedures. Although bone morphogenetic protein products in different matrices have been approved for decades, studies were of single-arm or open-label design.

METHODS: The study was a prospective, multicenter, double-blind, placebo-controlled randomized trial that enrolled 63 patients with degenerative disc disease (DDD) requiring single-level TLIF surgery. Patients were randomized 1:1:1 to 1 of 3 groups: placebo, 0.25mg, or 0.5mg AGA111. Investigational product was prepared by mixing AGA111 or placebo with ABC. The AGA111/ABC mixture was injected into the interbody area during TLIF surgery. All patients were followed for 12 months. Fusion was assessed by blinded adjudicators using CT scan images and hyperflexion/hyperextension X-rays at Months 3, 6, and 12. Functional outcomes and pain were assessed by Oswestry Disability Index (ODI) and pain visual analog scale (VAS) at Months 3, 6, and 12. Blood samples were evaluated for safety, pharmacokinetics, and anti-drug antibodies at multiple timepoints.

RESULTS: No patients were lost to follow-up. Both doses of AGA111 were safe and well-tolerated. The incidence of adverse events (AEs) was comparable between AGA111 and placebo. Fewer serious AEs were reported in AGA111-treated groups than placebo. No heterotopic ossification, seroma, deep wound infection, or radiculitis events were reported in patients treated with AGA111. At Month 3, fusion success rates of 21.1%, 42.1%, and 45% were observed for placebo, 0.25mg, and 0.5mg AGA111, respectively. At Month 6, fusion success rates of 60%, 73.7%, and 80% were observed for placebo, 0.25mg, and 0.5mg AGA111, respectively. At Month 12, fusion success rates of 90.5%, 89.5%, and 100% were observed for placebo, 0.25mg, and 0.5mg AGA111, respectively. At Month 3, ODI scores decreased by 22.8%, 18%, and 27.4% for placebo, 0.25mg, and 0.5mg AGA111, respectively. At Month 6, ODI scores decreased by 23.4%, 30.1%, and 33% for placebo, 0.25mg, and 0.5mg AGA111, respectively. At Month 12, ODI scores decreased by 24.4%, 31.7%, and 36.4% for placebo, 0.25mg, and 0.5mg AGA111, respectively. Similar trends were observed for pain VAS.

DISCUSSION AND CONCLUSION: AGA111 was safe and well-tolerated in patients with DDD undergoing single-level TLIF surgery. Compared to placebo, patients treated with AGA111 had higher rates of successful fusion and greater improvements in ODI and pain VAS, with the AGA111 0.5mg dose demonstrating better results compared to the 0.25mg dose, thus supporting further studies of AGA111 for spinal fusion.