ACTIFUSE Bone Graft Substitute Demonstrates Similar Fusion Rates to BMP-2 in Posterolateral Lumbar Fusion (PLF) Procedures

In a prospective, randomized, multicenter comparative study in 103 patients with degenerative spinal disorders requiring PLF (1-3 levels), ACTIFUSE Bone Graft Substitute provided fusion rates similar to BMP-2 (Level of Evidence:2).[1]

Key Points

- No significant difference in successful fusion between ACTIFUSE Bone Graft Substitute and BMP-2 [INFUSE Bone Graft] at 12 and 24 months.
- Pain assessment (VAS Score) at 6 months was significantly reduced with ACTIFUSE vs. BMP-2.
- Successful neurological status was higher with ACTIFUSE vs. BMP-2 at 6 months.

Overview

Although autologous iliac crest bone has long been considered the gold standard bone graft in PLF, harvesting is associated with significant morbidity at the donor site and prolonged hospitalization. Hence, there is much interest in substitute biomaterials.[2,3]

ACTIFUSE Bone Graft Substitute is a silicate substituted calcium phosphate synthetic bone graft that combines an optimized osteoconductive scaffold with an aqueous polymer gel resulting in a moldable, cohesive material that facilitates rapid and sustained bone ingrowth. Recombinant human bone morphogenetic protein, in combination with a bovine type I collagen scaffold, or BMP-2 [INFUSE, Medtronic, Inc.], is a bone inductive agent.

Vertebral fusion success rates for ACTIFUSE and BMP-2 were assessed by Coughlan et al[1] following PLF using computed tomography (CT) scans evaluated by independent radiographic reviewers at 12 and 24 months. CT scans were graded according to the method of Glassman et al.[4] Clinical outcomes included pain scores on a visual analog scale (VAS), Oswestry Disability Index (ODI), SF-36 and adverse events.

Results

A total of 103 patients were enrolled and received treatment (ACTIFUSE, n=51; BMP-2, n=52); 96 patients completed the study. The per-protocol (PP) population, defined as all patients who completed the study without protocol deviations, comprised 62 patients with evaluable fusion results (ACTIFUSE, n=35; BMP-2, n=27) at the primary endpoint of 12-month follow-up. Baseline demographics were similar in both treatment groups.

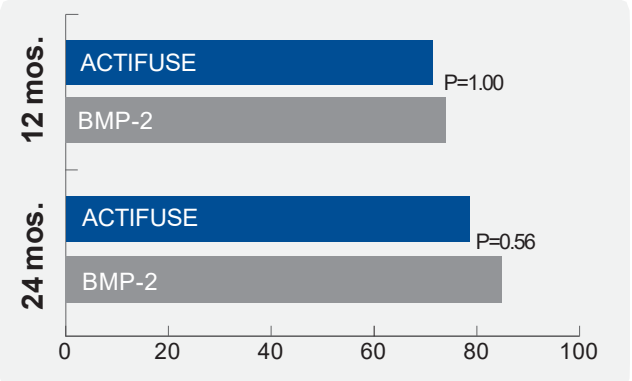
The primary diagnoses were spondylolisthesis (n=49;47.6%) and degenerative disc disease (n=46;44.7%). For most patients (n=74;71.8%), there was one involved vertebral level; 28 (27.2%) patients had two levels and one patient (1.0%) had three levels (**Table 1**).

Table 1. Primary Diagnoses/Vertebral Levels

Diagnosis/Level	Number/Percentage
Spondylolisthesis	n=49/47.6%
Degenerative Disc Disease	n=46/44.7%
One Level	n=74/71.8%
Two Levels	n=28/27.2%
Three level	n=1/1%

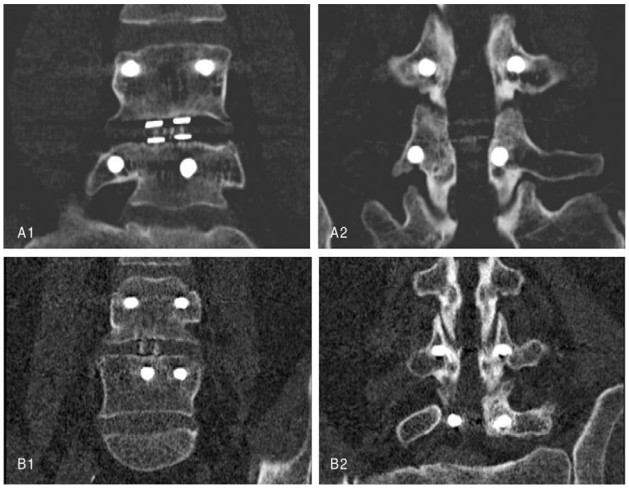
At 12 months, in the PP population (62 patients), fusion success was achieved in 25 of 35 (71.4%) in the ACTIFUSE group and in 20 of 27 (74.1%) in the BMP-2 group (P=1.00, **Figure 1**).

Figure 1. Proportion of PP patients with fusion success at 12 and 24 months.



Representative CT images of solid fusion at 12 months are shown in **Figure 2.** At 24 months in the PP analysis, fusions were noted in 78.6% and 84.8% of pateints in the ACTIFUSE and BMP-2 groups, respectively (P=0.56)(**Figure1**).

Figure 2. CT scans at 12 months. (A) Patient treated with ACTIFUSE (i) central section (ii) outer section. (b) Patient treated with BMP-2 (i) central section (ii) outer section.



For both treatment groups, mean VAS scores for back pain were lower than preoperative VAS scores for all subsequent time-points (**Figure 3**); at 6 months, the ACTIFUSE VAS scores were significantly lower than the BMP-2 group. **Table 2** summarizes ODI scores in the two treatment groups throughout the study. In the ACTIFUSE and BMP-2 groups, ODI score and SF-36 showed steady improvements over time (SF-36 significant at 6 months). At all time-points, the proportion of patients deemed as experiencing neurological success was higher in the ACTIFUSE vs. BMP-2 group (**Figure 4**), although the difference was not significant, except for the 6-month timepoint. The numbers and frequencies of AEs were similar between the two treatment groups. The most frequently reported AE was pain, followed by wound secretion, pain in an extremity, back pain, nausea and procedural pain.

Figure 3. Mean visual analog scale (VAS) scores up to 24 months after treatment with ACTIFUSE or BMP-2.

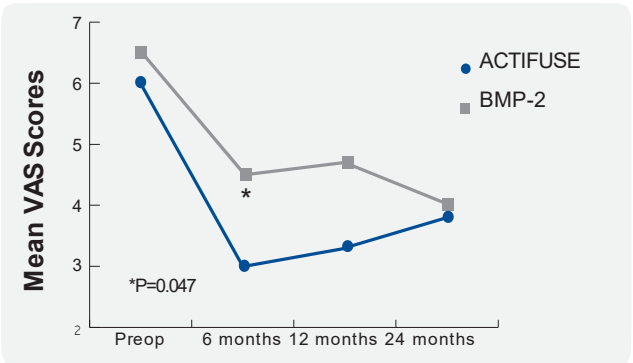
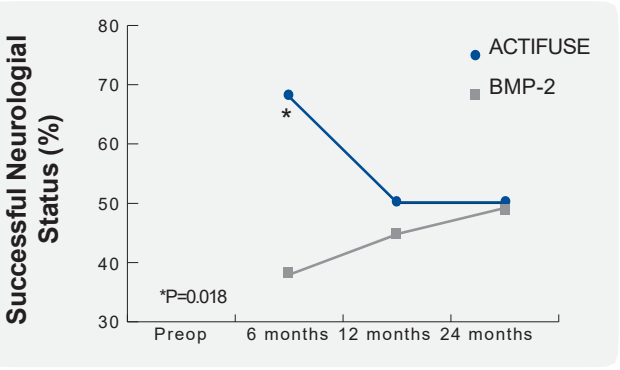


Table 2. Oswestry Disability Index (ODI) Scores

VISIT	ACTIFUSE	BMP-2
Preoperative	48.5±16.6 (n=47)	48.5±16.1 (n=35)
6 weeks	41.8±15.9 (n=36)	47.1±17.6 (n=25)
3 months	33.7±18.0 (n=36)	36.3±20.9 (n=30)
6 months	28.3±17.2 (n=40)	36.1±20.5 (n=29)
12 months	29.4±18.8 (n=41)	36.6±22.6 (n=32)
24 months	29.1±21.0 (n=39)	29.6±21.0 (n=27)

Figure 4. Neurological status up to 24 months after treatment with ACTIFUSE or BMP-2.



Discussion and Conclusions

Although BMP-2 has not gained FDA approval for use in PLF, it has been demonstrated as highly efficacious at inducing bone ingrowth in humans.[5–7] In patients undergoing PLF, equivalent bone fusion success was achieved using BMP-2 compared with control patients receiving iliac crest bone graft.[8]

The study was underpowered due to the number of patients who could not be included in the PP population. This was in part due to the number os protocol deviations, mostly arising from the omission of bulkiing agent to the BMP-2 material.

ACTIFUSE was safe and well tolerated in this study and provided fusion rates similar to those observed in patients receiving BMP-2 bone graft material. On the basis of historical control data, ACTIFUSE may be as useful as iliac crest bone autograft in the context of spine fusion surgery, with less risk of unwanted donor site morbidity.

References

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This study was funded by Baxter Healthcare.

UKI/MG95/19-0006 December 2019

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