

Appendix 1 Table P. Off-Label Comparative Study Quality of Life and Satisfaction Outcomes

| Investigator (yr, country, ref #) | Study design | Comparisons No. pts (BMP dose) | Patient diagnosis | Surgical intervention | Outcome measure mean score | Outcome measure % improved or success (p-value) | Comment |
|--|----------------------------------|---|----------------------------|---|-------------------------------|---|--|
| Boden et al., 2002 USA (84) Lumbar Spine | Multicenter nonblinded RCT | rhBMP2/CRM plus Texas Scottish Rite Hospital (TSRH) Spinal System (TSRHSS) n=11 | single-level lumbar DDD | single-level primary instrumented posterolateral lumbar fusion plus rhBMP2 ICBG | NR | Patient satisfaction (% good/excellent) pre, 1.5, 3, 6, 17 mos rhBMP2/CRM/TSRHSS 0, ~75, ~58, ~60, ~60 | Patient satisfaction measurements generally paralleled results of SF-36 pain survey and Oswestry DI |
| | | (40 mg/pt) rhBMP2/CRM alone n=11 | | | | Physician impression (% good/excellent) pre, 1.5, 3, 6, 17 mos rhBMP2/CRM/TSRHSS 0, ~90, ~80, ~80, ~80 | |
| | | (40 mg/pt) ICBG plus TSRHSS n=5 | | | | Patient satisfaction (% good/excellent) pre, 1.5, 3, 6, 17 mos rhBMP2/CRM alone 0, ~100, ~88, ~88, ~100 | |
| | | | | | | Physician impression (% good/excellent) pre, 1.5, 3, 6, 17 mos rhBMP2/CRM alone 0, ~100, ~85, ~80, ~85 | |
| | | | | | | Patient satisfaction (% good/excellent) pre, 1.5, 3, 6, 17 mos ICBG/TSRHSS 0, ~80, ~60, ~80, ~60 | |
| | | | | | | Physician impression (% good/excellent) pre, 1.5, 3, 6, 17 mos ICBG/TSRHSS 0, ~60, ~80, ~60, ~60 | |

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| <p>Burkus et al., 2005 USA (85) Lumbar Spine Note: includes all pts from Burkus et al., 2002, rec# 11510; same pts as Burkus et al., 2006, rec# 6640</p> | <p>Multicenter, nonblinded RCT</p> | <p>rhBMP2 n=79 (8-12 mg/pt)</p> | <p>single-level lumbar lumbar DDD</p> | <p>primary single-level anterior lumbar fusion with a pair of threaded allograft cortical bone dowels (CBD) plus rhBMP2 or ICBG</p> | <p>NR</p> | <p>NR</p> | |
| <p>Dimar et al., 2009 USA (86) Lumbar Spine Note: contains pts in Glassman et al., 2007, rec# 4040; Dimar et al., 2006 rec# 5480; Glassman et al., 2005, rec# 8040</p> | <p>Multicenter nonblinded RCT</p> | <p>rhBMP2/CRM n=239 (40 mg/pt)</p> | <p>single-level lumbar DDD</p> | <p>single-level primary instrumented posterolateral lumbar fusion plus rhBMP2 or ICBG</p> | <p>NR</p> | <p>NR</p> | |
| <p>Glassman et al., 2007 USA (99) Lumbar Spine</p> | <p>Retrospective with historical control group</p> | <p>rhBMP2 n=91 (12 mg/pt)</p> | <p>single- and multi-level lumbar DDD, degenerative scoliosis, postdissectomy instability, spinal stenosis, adjacent level degeneration</p> | <p>single- or multi-level primary or revision instrumented posterolateral lumbar fusion</p> | <p>NR</p> | <p>NR</p> | <p>Study only reported fusion data</p> |
| <p>Glassman et al., 2008 USA (87)</p> | <p>Multicenter nonblinded RCT</p> | <p>rhBMP2/ACS n=50 (dose not reported)</p> | <p>single- or multi-level lumbar DDD</p> | <p>single- or multi-level primary instrumented posterolateral</p> | <p>NR</p> | <p>NR</p> | |

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| Lumbar Spine | | ICBG n=52 | | lumbar fusion plus rhBMP2 or ICBG | | | |
| Haid et al., 2004 USA (88) Lumbar Spine | Multicenter, nonblinded RCT | rhBMP2 n=34 (4.2-8.4) | single-level lumbar DDD | single-level primary posterior lumbar interbody fusion (PLIF) interbody fusion cages plus rhBMP2 or ICBG | | Patient satisfaction at 24 mos rhBMP2 72 | Patient satisfaction rates comprise results for pts who report definitely and mostly true that they were satisfied with their surgical outcomes |
| | | ICBG N=33 | | | | ICBG 80 | |
| Johnsson et al., 2002 Sweden (92) Lumbar Spine | Multicenter nonblinded RCT | rhBMP7 n=10 (7 mg/pt) | single-level lumbar DDD | single-level primary uninstrumented posterolateral lumbar fusion with rhBMP7 or ICBG | NR | NR | |
| | | ICBG n=10 | | | | | |
| Kanayama et al., 2006 Japan, Cleveland (93) Lumbar Spine | Multicenter nonblinded RCT | rhBMP7 n=9 (7 mg/pt) | single-level lumbar DDD | single-level primary instrumented posterolateral lumbar fusion with rhBMP7 or AGB/CRM | NR | NR | |
| | | AGB/CRM n=10 | | | | | |
| Mummaneni et al., 2004 USA (100) Lumbar Spine | Retrospective single-center cohort study | rhBMP2/AGB n=25 (8.4 mg/pt) | single- or multi-level lumbar DDD | single- or multi- level primary transforaminal lumbar interbody fusion (TLIF) with interbody fusion cages with rhBMP2 plus AGB or ICBG alone | Prolo Scale Economic status subscale Mean score at F/U rhBMP2/AGB 3.8±0.8 | NR | Statistical analysis not done |
| | | | | | Medication use subscale Mean score at F/U rhBMP2/AGB 3.8±0.9 | | |

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| | | ICBG N=19 | | | Prolo Scale Economic status subscale Mean score at F/U ICBG 4.1±0.7 | | |
| | | | | | Medication use subscale Mean score at F/U ICBG 4.2±0.8 | | |
| Pradhan et al., 2006 USA (101) Lumbar Spine | Prospective consecutive patient single- center cohort study | rhBMP2 n=9 (dose NR) | single-level lumbar DDD | single-level primary anterior lumbar interbody fusion (ALIF) with femoral ring allograft (FRA) plus rhBMP2 or ICBG | NR | NR | Study only reported fusion data |
| | | ICBG n=27 | | | | | |
| Singh et al., 2006 USA (102) Lumbar Spine | Prospective single-center case-matched cohort study | rhBMP2/ICBG n=39 (12-36 mg/pt) | single- or multi-level lumbar DDD | single- or multi- level primary instrumented posterolateral lumbar fusion with rhBMP2 plus ICBG or ICBG alone | NR | NR | |
| | | ICBG N=11 | | | | | |
| Slosar et al., 2007 USA (103) Lumbar Spine | Prospective consecutive patient single- center cohort study | rhBMP2 n=45 (3-9 mg/pt) | single- or multi-level lumbar DDD | single- or multi- level primary instrumented anterior lumbar interbody fusion | NR | Patient satisfaction at 24 mos rhBMP2 86 | None of the pts who underwent revision fusions in ALG group expressed satisfaction with their outcomes |

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| | | ALG N=30 | | (ALIF) with femoral ring allograft (FRA) plus rhBMP2 or allograft bone chips (ALG) | | ALG 79 | |
| Vaccaro et al., 2008 USA (94) Lumbar Spine | Multicenter nonblinded RCT | rhBMP7 n=207 (7 mg/pt) | single-level lumbar DDD | single-level primary uninstrumented posterolateral lumbar fusion with rhBMP7 or ICBG | NR | NR | |
| | | ICBG n=86 | | | | | |
| Vaccaro et al., 2008 USA (95) Lumbar Spine Note: Long-term F/U study that includes all pts from Vaccaro et al., 2004 (184), and Vaccaro et al., 2005, (185) | Multicenter, nonblinded RCT | rhBMP7 n=24 (7 mg/pt) | single-level lumbar DDD | single-level primary uninstrumented posterolateral lumbar fusion with rhBMP7 or ICBG | NR | Patients in both groups displayed increases in the SF-36 mental health component subscale, increasing from the 25th percentile, reaching age- matched normative values at 48 mos. (data not shown) | |
| | | ICBG n=12 | | | | | |
| Baskin et al., 2003 USA (89) Cervical Spine | Multicenter, nonblinded RCT | rhBMP2/ALG n=18 (0.6-1.2 mg/pt) | single- or two-level cervical DDD | single- or two- level primary instrumented ACDF with rhBMP2/ALG or ICBG/ALG | NR | Patient satisfaction 24 mos > 90% in both groups | Patient satisfaction related to whether they were satisfied with their results, whether they were helped as much as anticipated, and whether they would have the surgery again |
| | | ICBG/ALG n=15 | | | | | |
| Butterman et al., 2008 USA (104) Cervical Spine | Prospective nonrandomized cohorts of consecutive patients | rhBMP2/CRA n=30 (0.9-3.7 mg/pt) | single- or multiple-level cervical DDD | single- or multi- level primary instrumented or uninstrumented ACDF with | NR | Patient-reported success 13-24, 25-36 mos rhBMP2/CRA 90, 89 | Patient satisfaction related to whether they were satisfied with their results, whether they would have the surgery |

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| | | ICBG n=36 | | rhBMP2/CRA or ICBG | | ICBG 94, 97 | again, and whether they would recommnd ot to others (97% in both groups) |
| Crawford et al., 2009 USA (105) Cervical Spine | Retrospective cohort of consecutive patients | rhBMP2/BGE n=41 (4.2-12 mg/pt) ICBG n=36 | single- or multi-level posterior cervical stenosis, ACDF nonunion, or unstable spondylosis | single- or multi- level instrumented posterior cervical spinal fusion with rhBMP2/BGE or ICBG | NR | NR | |
| Smucker et al., 2006 USA (106) Cervical Spine | Retrospective case-control | rhBMP2/CRA n=69 (dose NR) CRA n=165 | NR | single- or multi- level instrumented ACDF with rhBMP2/CRA or CRA alone | NR | NR | |
| Vaidya et al., 2007 USA (107) Cervical Spine | Retrospective cohort of consecutive patients | rhBMP2 n=22 (1-3 mg/pt) ALG/DBM n=24 | single- or multiple-level cervical DDD with radiculopathy or myelopathy | single- or multi- level primary instrumented ACDF with interbody fusion cages rhBMP2 on ACS or ALG/DBM | NR | NR | |
| Boraiah et al., 2009 USA (108) Acute Tibial Fractures | Retrospective case series | rhBMP2 (1) n=17 (12 mg/pt) (2) n=23 no BMP | Complex tibial plateau fractures | Surgery for Acute traumatic tibial plateau fractures | NR | NR | |
| Jones et al., 2006 USA (90) Acute Tibial Fractures | Multicenter prospective RCT | rhBMP2 (1) n=15 (12 mg/pt with allograft bone chips | Diaphyseal tibial fracture with cortical defects | Reconstruction of diaphyseal tibial fractures with cortical defect | NR | NR | |

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| | | (2) n=15 autogenous bone graft | | | | | |
| Ristiniemi et al., 2007 Finland (110) Acute Tibial Fractures (same pts as rec#4560) | Retrospective cohort of matched patients | Rh-BMP7 N=20 | Distal tibial fracture (OTA zone 43) treated with external fixation | Distal tibial fracture (OTA zone 43) treated with external fixation by BMP7 and graft | Iowa Ankle Score: BMP: 84(70 to 100) | NR | |
| | | Matched Zone 43 fracture (OREF) N=20 | | | Matched: 81.6 (46 to 98) P=.6 | | |
| Bilic et al., 2006 Croatia, Netherlands (96) Miscellaneous Off- Label Uses | Single-center, unblinded RCT | rhBMP7/AGB n=6 (3.5 mg/pt) | symptomatic proximal pole scaphoid nonunion | revision of nonunion | NR | NR | |
| | | rhBMP7/ALG n=6 (3.5 mg/pt) | | | | | |
| | | ICBG n=6 | | | | | |
| Dickinson et al., 2008 USA (91) Miscellaneous Off- Label Uses | Single-center RCT | rhBMP2/ACS n=9 (dose not given) | unilateral cleft lip- palate with an alveolar cleft defect | repair of unilateral cleft lip-palate with an alveolar cleft defect | NR | NR | |
| | | ICBG n=12 | | | | | |
| Ekrol et al., 2008 UK (97) Miscellaneous Off- Label Uses | Prospective randomized cohort | rhBMP2 Non bridging external fixation N=4 | Osteotomy of the distal radius for symptomatic malunion (with and without external fixation) | Osteotomy of the distal radius for symptomatic malunion (with and without external fixation) with RhBMP-7 and autologous bone graft | NR | NR | |
| | | Bone graft Non bridging external fixation N=6 | | | | | |
| | | RhBMP-7 internal fixation w/ pi-plate N=10 | | | | | |

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| | | Bone graft internal fixation w/ pi-plate N=10 | | | | | |
| Geesink et al., 1999 Netherlands (98) Miscellaneous Off- Label Uses | Prospective double-blind randomized study | Untreated N=6 DMB N=6 Collagen type I N=6 OP-1 (2.5mg) with Collagen type I N=6 | High tibial osteotomy | High tibial osteotomy with three osteoinductive materials | HSS mean score increased in all groups over time and was comparable at every followup. 68 before operation and 90 post- op | 21 overall satisfied, 3 not satisfied. 1 unsatisfied in untreated, 1 op-1, 1 DMB | |
| Karrholm et al., 2006 UK (111) Miscellaneous Off- Label Uses | Single-center case-control | Cups rhBMP7/ALG (1 g/pt) n=10 Cups ALG n=10 Stems rhBMP7/ALG (1 g/pt) n=11 Stems ALG n=30 | required revision of total hip arthroplasty | impaction grafting for revision of hip arthroplasty | NR | NR | |
| Maeda et al., 2009 USA, Japan (109) | Cohort study with nonconcurrent control group | rhBMP2/BGE n=23 (64-320 mg/pt) ICBG n=32 | spinal deformity | primary instrumented posterior spinal fusion from thoracic spine to the sacrum or ilium, or anterior fusion between same locations using interbody fusion cage | NR | NR | |