

**Appendix 1 Table C. On-Label Comparative Studies Patient Characteristics**

Investigator (yr, country, ref #) Surgical Site	Study design	Comparison(s) No. pts (BMP dose)	Patient diagnosis	Surgical intervention	Defect severity and characteristics (%)	Age mean ± SD yrs (rng)	≥ 65 yrs (%)	Males (%)	Weight mean ± SD lbs (rng)	Comorbidities (%)	Comment
Boden et al., 2000 USA (71) <b>Lumbar Spine</b>	Multicenter, nonblinded RCT	rhBMP2 (4.2-8.4 mg/pt) n=11	single-level lumbar DDD	single-level primary anterior lumbar fusion with interbody fusion cages plus rhBMP2 or ICBG	grade I spondylolisthesis	rhBMP2 42±3 (30-62)	NR	rhBMP2 46	rhBMP2 166±11 (125-228)	Tobacco use rhBMP2 0 Frequent alcohol use rhBMP2 36.4	No significant differences between groups
		ICBG n=3				ICBG 40±0.6 (38-42)		ICBG 67	ICBG 211±11 (190-249)	Tobacco use ICBG 33.3 Frequent alcohol use ICBG 33.3	
Burkus et al., 2002 USA (72) <b>Lumbar Spine</b>	Multicenter, nonblinded RCT	rhBMP2 (4.2-8.4 mg/pt) n=143	single-level lumbar DDD	single-level primary anterior lumbar fusion with interbody fusion cages plus rhBMP2 or ICBG	NR	rhBMP2 43	NR	rhBMP2 54	rhBMP2 179	Tobacco use rhBMP2 33	No significant differences between groups
		ICBG n=136				ICBG 42		ICBG 50	ICBG 181	ICBG 36	
Burkus et al., 2003 USA (182) <b>Lumbar Spine</b>	Retrospective comparative analysis	rhBMP2 n=277 (dose NR)	single-level lumbar DDD	single-level primary anterior lumbar fusion with interbody	NR	rhBMP2 42±10	NR	rhBMP2 48.7	rhBMP2 175±36	Tobacco use rhBMP2 31.4 Alcohol use rhBMP2	Other significant differences include previous back

Note: may include pts in Burkus et al., 2003 (80)				fusion cages						37.9	surgeries (lower in ICBG group), use of non-narcotic, weak narcotic, and muscle relaxant medications (all higher in rhBMP2 group)		
		ICBG n=402				ICBG 41±10				ICBG 52.2		ICBG 179±38	Tobacco use ICBG 32.8
						p=0.007							Alcohol use ICBG 34.1
Dawson et al., 2009 USA (73) <b>Lumbar Spine</b>	Multicenter nonblinded RCT	rhBMP2/CRM n=25 (12 mg/pt)	single-level lumbar DDD	single-level primary instrumented posterolateral lumbar fusion plus rhBMP2 or ICBG	grade I spondylolisthesis	rhBMP2/CRM 56	NR	rhBMP2/CRM 40	rhBMP2/CRM 176	Tobacco use rhBMP2/CRM 24 ICBG 24 Previous back surgery rhBMP2/CRM 24 ICBG 29	Previous back surgery not at index level		
		ICBG n=21				ICBG 57		ICBG 43	ICBG 185				
Govender et al. for the BESTT study group 2002 South Africa (74) <b>Open Tibial Fractures</b>	Multi-center, single blind, RCT	rhBMP2 n=151 (6 mg/patient)	Open tibial fracture where the major component was diaphyseal	IM nail fixation and soft tissue management	Gustilo-Anderson Types I (29), II (51), IIIA (43), IIIB (22)	37 (17-78)	NR	364 (81%)	NR	Tobacco Use 73 (50%)			
		rhBMP2 n=149 (12 mg/patient)				I(32), II(50), IIIA (38), IIIB (25)						33 (18-77)	75 (52%)
		n=150				I (34), II (54)						37 (17-87)	66 (45%)

		Standard care (IM nail fixation and soft tissue management )			IIIA (42), IIIB (17)						
Swiontkowski et al., 2006 USA (81) <b>Open Tibial Fractures</b> Note: This paper reports on 131 of the same patients included in Govender et al., 2002 (74)	Subgroup analysis of combined data from two prospective randomized trials with identical designs	rhBMP2 (1) n=169 (12 mg/patient)	Acute open tibial fracture	IM nail fixation and soft tissue management	Gustilo-Anderson Types (1) BESTT, I (21.1%) II, (33.6%), IIIA and IIIB (44%) USS, I(15%), II(45%), IIIA and IIIB (40%)	(1) BESTT, 33.4 years USS, 35.2 years	NR	(1) BESTT, 84.6% USS, 85%	(1) BESTT, 166 USS,193	Smokers (1) BESTT, 51.7% USS,40%	
		(2) n=169 Standard care (IM nail fixation and soft tissue management )			(2) BESTT, I (23.3%), II (36.7%), IIIA and IIIB, 40.6%) USS, I (15.8%), II(31.6%), IIIA and IIIB, (52.6%)	(2) BESTT, 36.8 years USS, 33.6 years		(2) BESTT, 78.7% USS, 89.5%	(2) BESTT, 166 USS, 176	(2) BESTT, 44.9% USS, 52.6%	
Boyne et al., 2005 USA (75) <b>Maxillofacial and Dental</b>	Multicenter randomized dose-comparison, safety and efficacy study	rhBMP2/ACS (6-24 mg/pt) n=18	< 6 mm alveolar bone height in the posterior maxilla	staged bilateral or unilateral maxillary sinus floor augmentation	Partially/totally edentulous rhBMP2/ACS 0.75 mg/mL 72/28	rhBMP2/ACS 0.75 mg/mL 57±12	NR	rhBMP2/ACS 0.75 mg/mL 44	rhBMP2/ACS 0.75 mg/mL 151±32	Alcohol use rhBMP2/ACS 0.75 mg/mL 44	No significant differences between groups
		rhBMP2/ACS (15-48 mg/pt) n=17			rhBMP2/ACS 1.50 mg/mL 59/41	rhBMP2/ACS 1.50 mg/mL		rhBMP2/ACS 1.50 mg/mL	rhBMP2/ACS 1.50 mg/mL	rhBMP2/ACS 1.50 mg/mL	

						52±9		35	157±32	53	
		AGB n=13			AGB 69/31	AGB 57±11		AGB 38	AGB 164±52	AGB 46	
Fiorellini et al., 2005 USA (76) <b>Maxillofacial and Dental</b>	Double-blind, multicenter randomized, placebo-control dose-comparison, safety and efficacy study	rhBMP2/ACS (mn dose 0.9 mg/pt) n=22  (mn dose 1.9 mg/pt) n=21  Placebo n=17  No Tx n=20	≥ 50% buccal bone loss of the extraction socket(s)	extraction socket augmentation	NR	47 (all pts)	NR	54 (all pts)	NR	NR	Poorly described demographics
Triplett et al., 2009 USA (77) <b>Maxillofacial and Dental</b>	Multicenter nonblinded RCT	rhBMP2/ACS n=80 (12-24 mg/pt)  AGB n=80	< 6 mm alveolar bone height in the posterior maxilla	staged bilateral or unilateral maxillary sinus floor augmentation	Partially or totally edentulous, not reported	rhBMP2/ACS 54 (23-76)  AGB 51 (24-75)	rhBMP2/ACS 21  AGB 8  (p=0.024)	rhBMP2/ACS 56  AGB 32  (p=0.003)	NR	NR	
van den Bergh et al., 2000 Netherlands (82) <b>Maxillofacial and Dental</b>	Retrospective cohort study	rhBMP7/ACS n=3 (2.5 mg/pt)  ICBG n=3	partly edentulous	maxillary sinus floor augmentation	NR	rhBMP7/ACS 54±5  ICBG 53±5	0	rhBMP7/ACS 33  ICBG 33	NR	NR	
Calori et al., 2008 Italy (78)	Single-center, nonblinded RCT	rhBMP7/ACS n=60 (3.5-7.0 mg/pt)	post-traumatic atrophic nonunion	open reduction internal fixation	rhBMP7 15 tibial, 10 femoral, 12 humeral, 12 )	rhBMP7 md 44 (19-65)	NR	rhBMP7 53	NR	Tobacco use rhBMP7 33	No significant differences between

<b>Long Bone Nonunion</b>			for $\geq 9$ mos, with no signs of healing over the last 3 mos	(ORIF), external fixation (EF), or reamed intramedullary nailing (IM) with rhBMP7 or PRP	ulnar, 8 radial						groups
		4 open at injury, (1 Gustilo grade II, 2 grade IIIa, 1 grade IIIb)			md duration 20 $\pm$ 2 mos						
		PRP n=60			PRP 19 tibial, 8 femoral, 16 humeral, 8 ulnar, 9 radial	PRP md 41 (21-62)		PRP 58			Tobacco use PRP 28
					5 open at injury (1 Gustilo grade I, 1 grade II, 2 grade IIIa, 1 grade IIIb)						Previous surgery PRP md 2 (1-5)
					md duration 19 $\pm$ 3 mos						
					prior autograft 35%						
<b>Long Bone Nonunion</b>	Retrospective cohort study	rhBMP7/ACS n=15 (3.5 mg/pt)	tibial fracture nonunion with clinical and radiographic failure to progress to union for $\geq 9$	open reduction internal fixation (ORIF), exchange intramedullary nailing (IM), or Ilizarov, with rhBMP7 or	rhBMP7/ACS Gustilo II, IIIa, IIIb 4 (27)	rhBMP7/ACS 41 (16-64)	NR	rhBMP7/ACS 67	NR	NR	No significant differences between groups
		ICBG n=12			ICBG Gustilo II, IIIb 4 (33)	ICBG 38 (20-79)		ICBG 75			

			mos. following initial fracture stabilization	ICBG							
Friedlaender et al., 2001 (79) <b>Long Bone Nonunion</b>	Multicenter, partially blinded RCT	rhBMP7/ACS n=61 (3.5-7.0 mg/pt)	tibial nonunion for ≥ 9 mos, with no signs of healing over the last 3 mos	IM rod fixation with rhBMP7/ACS or AGB	rhBMP7/ACS atrophic nonunion 25 (41%)	rhBMP7/ACS 38±16	NR	rhBMP7/ACS 67	rhBMP7/ACS 171±47	Tobacco use rhBMP7/ACS 74	No significant differences between groups except proportion of atrophic nonunions
		comminuted fracture at injury 41 (67%)									
		open fracture at injury 35 (58%)									
		Gustilo grade III, IIIa, IIIb, or IIIc at injury 18 (30%)									
		md duration 27±26 mos									
		prior autograft 26 (43%)									
		prior IM rod 33 (54%)									
		AGB n=61			AGB atrophic nonunion 15 (25%) (p=0.048)						
comminuted fracture at											

					injury 34 (56%)						
					open fracture at injury 35 (57%)						
					Gustilo grade III, IIIa, IIIb, or IIIc at injury 22 (36%)						
					md duration 33±46 mos						
					prior autograft 19 (31%)						
					prior IM rod 27 (44%)						