

Table 14.2.10.1
Summary of Pharmacodynamic Parameters - Bone Turnover
Safety Population

Parameter: Procollagen 1 N-Terminal Propeptide (ng/mL)

Visit	Statistic	Treatments				Total (N=48)
		Dose Group 1 0.25 mg/kg/day (N=12)	Dose Group 2 0.75 mg/kg/day (N=12)	Dose Group 3 2.0 mg/kg/day (N=12)	Dose Group 4 6.0 mg/kg/day (N=12)	
Baseline	n	12	11	12	12	47
	Mean	555.8	480.7	508.2	511.5	514.7
	SD	184.72	118.20	94.36	106.50	129.49
	Median	493.5	519.0	534.5	516.0	510.0
	Minimum	351	344	336	350	336
	Maximum	1024	663	652	696	1024
	Interquartile Range	470.0, 558.5	359.0, 582.0	437.5, 571.5	422.5, 571.5	417.0, 576.0
Day 1	n	12	12	12	11	47
	Mean	474.0	443.7	417.1	475.2	452.0
	SD	116.45	112.38	87.35	147.10	115.68
	Median	454.5	467.5	413.0	483.0	431.0
	Minimum	262	207	267	213	207
	Maximum	668	637	551	722	722
	Interquartile Range	405.5, 542.0	373.5, 516.0	353.0, 488.5	386.0, 531.0	383.0, 518.0

(1) Percentage change is calculated as $100 \times (\text{change from baseline} / \text{baseline})$.
Baseline is defined as the last response during Screening prior to Study Day -1. P-values are from paired t-tests testing statistical significance of the change from baseline.

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Day 1 Change from Baseline	n	12	11	12	11	46
	Mean	-81.8	-34.5	-91.1	-36.5	-62.1
	SD	124.24	101.97	64.64	144.04	111.30
	Median	-60.0	-34.0	-107.5	-116.0	-70.5
	Minimum	-371	-168	-174	-182	-371
	Maximum	80	177	15	276	276
	Interquartile Range	-138.5, 13.0	-125.0, 32.0	-143.5, -35.0	-142.0, 85.0	-142.0, 5.0
	P-Value	0.0436	0.2874	0.0005	0.4209	0.0005
Day 1 Percent change from Baseline (1)	n	12	11	12	11	46
	Mean	-12.2	-5.4	-17.4	-5.7	-10.4
	SD	17.07	24.58	12.59	30.76	21.90
	Median	-12.3	-6.2	-19.6	-21.1	-15.5
	Minimum	-36	-44	-35	-39	-44
	Maximum	16	51	4	66	66
	Interquartile Range	-25.0, 2.7	-20.4, 9.1	-26.3, -6.2	-26.1, 19.9	-25.3, 1.4

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Week 2	n	12	12	12	12	48
	Mean	443.8	407.8	346.6	303.7	375.5
	SD	93.86	96.54	68.59	56.38	95.26
	Median	438.0	385.0	347.0	314.5	363.5
	Minimum	242	291	253	188	188
	Maximum	607	597	442	367	607
	Interquartile Range	394.5, 490.5	342.5, 440.5	276.0, 410.5	272.5, 346.0	308.5, 432.0
Week 2 Change from Baseline	n	12	11	12	12	47
	Mean	-112.0	-70.6	-161.6	-207.8	-139.4
	SD	125.08	123.69	73.52	78.16	111.79
	Median	-87.5	-68.0	-159.0	-200.0	-137.0
	Minimum	-417	-205	-297	-361	-417
	Maximum	25	241	-43	-90	241
	Interquartile Range	-150.5, -24.0	-189.0, -29.0	-215.5, -112.5	-229.0, -164.0	-205.0, -66.0
	P-Value	0.0101	0.0875	<.0001	<.0001	<.0001

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Week 2 Percent change from Baseline (1)	n	12	11	12	12	47
	Mean	-17.5	-11.2	-30.9	-39.9	-25.2
	SD	14.65	29.19	11.80	9.22	20.43
	Median	-18.2	-18.2	-29.3	-41.0	-28.6
	Minimum	-41	-36	-52	-52	-52
	Maximum	5	70	-11	-22	70
	Interquartile Range	-29.8, -4.8	-33.4, -7.9	-38.9, -23.1	-46.6, -33.0	-39.0, -18.1
Week 4	n	12	12	12	12	48
	Mean	573.8	496.7	492.0	566.3	532.2
	SD	251.02	117.57	81.92	149.32	162.01
	Median	491.0	486.5	488.0	584.5	511.0
	Minimum	350	287	369	321	287
	Maximum	1178	755	612	800	1178
	Interquartile Range	394.5, 658.5	437.0, 533.5	426.0, 552.5	461.5, 675.0	423.0, 608.5

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Week 4 Change from Baseline	n	12	11	12	12	47
	Mean	18.1	21.3	-16.2	54.8	19.5
	SD	153.10	122.87	79.64	118.09	119.99
	Median	-57.5	-41.0	-2.5	27.0	-2.0
	Minimum	-113	-137	-131	-107	-137
	Maximum	360	297	120	311	360
	Interquartile Range	-100.5, 108.5	-64.0, 109.0	-91.5, 37.5	-12.0, 81.5	-66.0, 59.0
	P-Value	0.6903	0.5785	0.4965	0.1360	0.2718
Week 4 Percent change from Baseline (1)	n	12	11	12	12	47
	Mean	2.8	7.8	-1.4	11.8	5.2
	SD	25.57	30.86	17.47	28.24	25.55
	Median	-10.3	-7.0	-0.4	4.3	-0.4
	Minimum	-23	-21	-26	-25	-26
	Maximum	46	86	36	75	86
	Interquartile Range	-16.6, 22.1	-12.7, 23.0	-16.3, 7.2	-2.9, 12.9	-13.4, 14.9

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