

Online Appendix Table 1. Changes in waist circumference, lipoprotein profiles, and blood pressure from baseline to Month 4 and from baseline to Month 12 (4-Mo and 12-Mo Evaluable Subjects)

	Pramlintide						
	Placebo	120 µg BID	120 µg TID	240 µg BID	240 µg TID	360 µg BID	360 µg TID
Waist (cm)							
Mo-4 Baseline	113.0±2.3	110.7±2.3	113.9±1.9	114.4±2.3	114.3±2.0	116.2±2.3	114.6±1.7
Change to Mo-4	-4.2±0.9	-4.8±0.9	-6.6±1.0*	-6.0±1.0	-6.9±1.0*	-6.7±1.0	-4.3±0.9
Mo-12 Baseline	110.0±3.5	109.2±2.4	115.8±2.4	114.2±3.6	113.0±3.0	114.3±3.1	114.0±3.1
Change to Mo-12	-4.1±2.1	-4.7±0.8	-7.9±1.8*	-10.0±3.0	-11.1±1.8**	-9.9±1.9**	-6.4±1.7
HDL-c (mg/dL)							
Mo-4 Baseline	50.8±2.1	51.9±2.3	53.0±2.5	49.3±2.5	49.6±1.9	49.5±2.1	53.5±1.9
Change to Mo-4	1.56±0.90	2.24±1.02	1.81±1.52	2.39±0.98	1.89±0.84	1.03±1.01	0.00±0.96
Mo-12 Baseline	51.7±3.2	52.0±3.2	50.6±2.4	48.3±3.2	54.3±2.7	50.0±3.6	56.6±3.1
Change to Mo-12	-0.50±1.56	3.65±1.69	4.48±1.74**	2.88±1.70	2.86±1.33	4.19±1.33	2.94±2.07
LDL-c (mg/dL)							
Mo-4 Baseline	128.1±5.7	118.5±4.9	117.8±6.0	119.9±5.2	120.3±4.2	121.7±5.2	123.8±4.7
Change to Mo-4	0.56±2.72	-1.22±2.99	-1.59±2.55	1.68±3.28	-4.43±2.65	-0.87±4.61	0.34±2.76
Mo-12 Baseline	131.8±8.4	113.2±6.0	115.3±8.7	119.1±8.3	126.8±5.8	124.3±7.4	121.8±5.2
Change to Mo-12	-4.63±5.37	2.48±4.74	-6.04±4.28	8.24±8.45	-2.71±4.00	-5.10±5.84	-0.19±4.37
Triglycerides (mg/dL)							
Mo-4 Baseline	133.7±7.5	127.7±10.4	129.3±11.5	117.4±9.3	133.0±8.5	139.1±12.4	125.3±8.8
Change to Mo-4	-2.29±5.96	5.00±10.44	-5.76±8.39	5.75±11.35	-14.64±6.94	-12.82±8.71	7.76±7.40
Mo-12 Baseline	153.8±17.6	132.5±14.4	124.3±15.8	129.1±12.7	135.2±14.0	156.3±19.6	115.9±8.4
Change to Mo-12	-4.38±10.69	14.09±10.50	-2.84±10.45	-0.59±10.50	-8.36±15.28	-17.24±21.87	-10.47±9.48
Systolic BP (mmHg)							
Mo-4 Baseline	124.1±2.5	121.1±1.9	123.4±2.1	120.4±2.0	123.9±2.2	126.6±1.9	120.2±1.6
Change to Mo-4	-1.9±1.8	-1.3±2.0	-1.0±2.3	-3.9±1.7	-2.5±1.8	-5.5±1.4	0.7±1.6
Mo-12 Baseline	122.7±3.3	122.1±2.7	124.4±2.4	118.4±2.8	121.7±3.0	126.7±2.6	121.9±2.6
Change to Mo-12	-0.3±3.2	0.3±3.1	-4.9±2.1	-1.5±2.7	-0.4±2.0	-7.3±3.1	3.5±2.6
Diastolic BP (mmHg)							
Mo-4 Baseline	77.4±1.7	76.4±1.2	79.0±1.2	77.2±1.4	78.8±1.1	79.4±1.3	78.0±1.1
Change to Mo-4	-1.1±1.4	-1.9±1.2	-1.3±1.4	-4.8±1.1*	-3.1±1.0	-2.4±1.2	-2.1±1.2
Mo-12 Baseline	79.5±1.8	77.2±1.6	78.5±1.4	76.3±1.6	77.0±1.6	80.8±1.6	79.4±1.7
Change to Mo-12	-0.4±2.8	2.4±2.1	-3.0±1.5	-0.9±2.0	0.1±2.0	-3.6±1.8	-0.6±2.3

Mean±SE; *P<0.05; **P<0.01 versus placebo

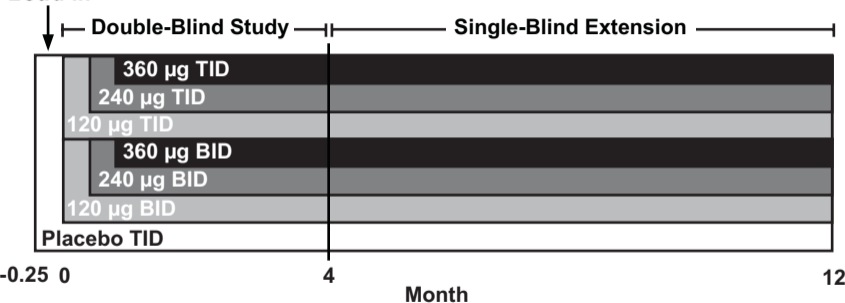
Online Appendix Table 2. Adverse events occurring at with an incidence $\geq 2.5\%$ and greater in the pooled pramlintide treatment group than with placebo (ITT)

	Placebo n (%)	Pramlintide						
		Pooled n (%)	120 μ g BID n (%)	120 μ g TID n (%)	240 μ g BID n (%)	240 μ g TID n (%)	360 μ g BID n (%)	360 μ g TID n (%)
Main Study (N = 408)								
Nausea	1 (1.7)	67 (19.2)	11 (18.6)	10 (16.9)	9 (16.7)	5 (8.9)	14 (23.7)	18 (29.0)
Diarrhea	2 (3.4)	15 (4.3)	2 (3.4)	3 (5.1)	3 (5.6)	1 (1.8)	3 (5.1)	3 (4.8)
Headache	0 (0.0)	15 (4.3)	6 (10.2)	2 (3.4)	2 (3.7)	1 (1.8)	0 (0.0)	4 (6.5)
Injection site bruising	1 (1.7)	12 (3.4)	2 (3.4)	2 (3.4)	2 (3.7)	4 (7.1)	1 (1.7)	1 (1.6)
Nasopharyngitis	1 (1.7)	10 (2.9)	0 (0.0)	0 (0.0)	1 (1.9)	2 (3.6)	5 (8.5)	2 (3.2)
Vomiting	0 (0.0)	9 (2.6)	1 (1.7)	4 (6.8)	0 (0.0)	1 (1.8)	2 (3.4)	1 (1.6)
Urinary tract infection	1 (1.7)	9 (2.6)	2 (3.4)	0 (0.0)	1 (1.9)	3 (5.4)	2 (3.4)	1 (1.6)
Extension (N = 209)								
Nasopharyngitis	2 (7.4)	17 (9.3)	1 (3.6)	3 (10.3)	4 (16.0)	2 (6.7)	5 (15.6)	2 (5.3)
Back pain	0 (0.0)	9 (4.9)	2 (7.1)	1 (3.4)	2 (8.0)	1 (3.3)	1 (3.1)	2 (5.3)
Nausea	0 (0.0)	7 (3.8)	0 (0.0)	1 (3.4)	1 (4.0)	0 (0.0)	3 (9.4)	2 (5.3)
Arthralgia	0 (0.0)	6 (3.3)	1 (3.6)	1 (3.4)	1 (4.0)	2 (6.7)	0 (0.0)	1 (2.6)
Depression	0 (0.0)	6 (3.3)	0 (0.0)	3 (10.3)	1 (4.0)	2 (6.7)	0 (0.0)	0 (0.0)
Diarrhea	0 (0.0)	5 (2.7)	0 (0.0)	1 (3.4)	1 (4.0)	1 (3.3)	1 (3.1)	1 (2.6)

Online Appendix Figure 1. Study Design. Following a one-week placebo lead-in, pramlintide treatment was initiated at 120 μ g and was increased by 120- μ g increments every 2-weeks until the assigned maintenance dose was reached (120, 240 or 360 μ g).

Online Appendix Figure 2. Changes in body weight (kg) from baseline (month 0) for BID (A,C) and TID (B,D) treated subjects who never reported nausea in the double-blind study (A-B)(ITT population; n = 340) and single-blind extension (C-D) (ITT population; n = 202) White circles = placebo; Pramlintide: black triangles = 120 μ g; white triangles = 240 μ g; black circles = 360 μ g. Mean \pm SE

**Placebo
Lead-In**



-0.25 0

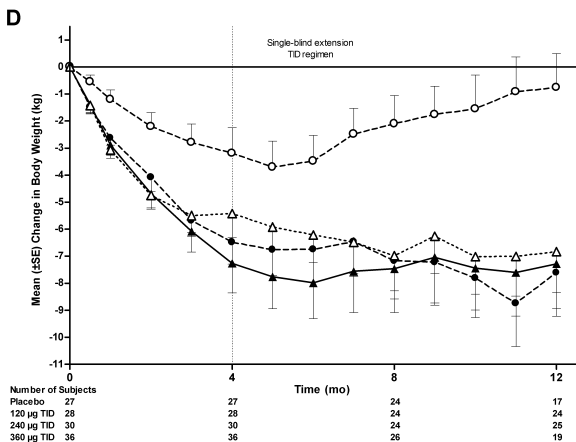
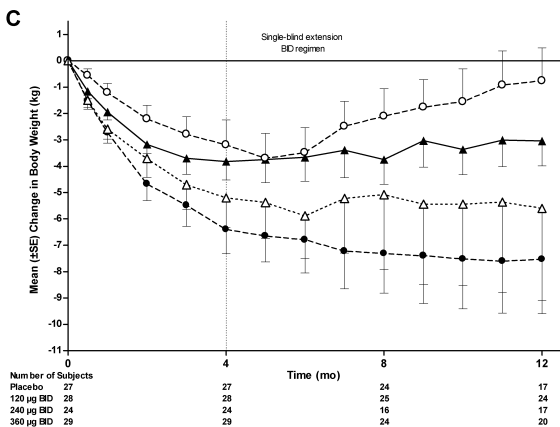
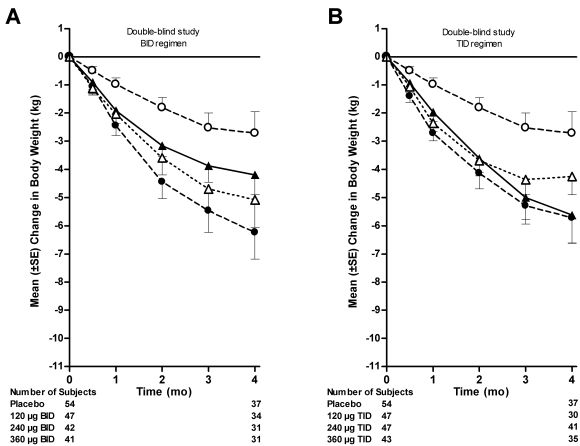
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12

Month

Weight Loss LSI

Weight Maintenance LSI



-○- Placebo --△-- 240 μ g Pramlintide
 -▲- 120 μ g Pramlintide -●- 360 μ g Pramlintide