TABLE .2

[illegible] STUDY NO. 301

[illegible] COMPARATIVE RESULTS
[illegible] LABORATORY DATA

Variable (Units)	Treatment Group	Completers Only						All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change	S.D.	Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
Specific Gravity (1.001-1.035)	PN 5 mg	28	1.021	0.006	0.001	0.006	0.000	0.007	37	1.021	0.006	0.000	0.006
	PN 10 mg	26	1.0[illegible]	0.004	0.003	0.007	-0.001	0.006	35	1.020	0.005	0.000	0.007
	PN 15 mg	34	1.020	0.006	0.00[illegible]	0.006	0.001	0.009	40	1.020	0.006	0.001	0.008
	PN 20 mg	31	1.023	0.005	-0.004*	0.007	-0.003*	0.008	37	1.022	0.006	-0.002(*)	0.008
	Placebo	31	1.022	0.005	-0.001	0.007	-0.002	0.007	38	1.023	0.006	-0.002	0.007
pH (5.0-7.0)	PN 5 mg	28	5.25	0.52	0.07	0.61	0.07	0.60	37	5.24	0.49	0.05	0.62
	PN 10 mg	26	5.17	0.49	-0.08	0.56	0.04	0.45	35	5.23	0.49	-0.03	0.51
	PN 15 mg	34	5.35	0.49	0.00	0.65	0.00	0.74	40	5.38	0.54	-0.05	0.78
	PN 20 mg	31	5.17	0.48	0.03	0.55	0.16	0.86	37	5.19	0.46	0.14	0.82
	Placebo	31	5.26	0.58	0.[illegible]	0.[illegible]	0.[illegible]	0.70	38	5.24	0.54	0.13	0.66

(*)p<0.[illegible] *p<.05, **p<.01, ***p<.001

TABLE 33

PN 2207-[illegible] STUDY NO. 301

SUMMARY COMPARATIVE RESULTS
FOR CHEMISTRY DATA

Variable (Normal Range)	Treatment Group	Completers Only							All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change	S.D.	Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
Calcium mg/dl (8.5-10.5)	PN 5 mg	32	9.63	0.36	0.05	0.30	-0.10	0.40	37	9.61	0.36	-0.05	0.44
	PN 10 mg	28	9.44	0.32	0.01	0.45	0.08	0.39	34	9.43	0.31	0.14(*)	0.42
	PN 15 mg	35	9.45	0.43	[illegible]	0.40	0.06	0.40	40	9.47	0.42	0.05	0.38
	PN 20 mg	32	9.[illegible]	[illegible]	0.06	0.28	0.02	0.35	39	9.46	0.35	0.02	0.36
	Placebo	30	9.39	0.39	0.10(*)	0.37	0.07	0.50	35	9.37	0.38	0.08	0.46
Inorganic Phosphorus mg/dl (2.7-4.5)	PN 5 mg	32	3.15	0.49	0.04	0.41	0.08	0.37	37	3.19	0.47	0.04	0.40
	PN 10 mg	28	3.25	0.49	0.02	0.53	.03	0.47	34	3.19	0.53	0.07	0.48
	PN 15 mg	35	3.09	[illegible]	-0.02	0.3[illegible]	-0.11	0.50	40	3.12	0.49	-0.09	0.48
	PN 20 mg	32	3.10	0.64	-0.04	0.62	-0.09	0.78	39	3.10	0.60	-0.04	0.76
	Placebo	30	3.02	0.66	0.12	0.62	0.00	0.65	35	3.05	0.62	0.01	0.61
BUN mg/dl (6-23)	PN 5 mg	32	13.2	4.22	0.15	4.15	2.66	3.62	37	13.4	4.10	0.62	3.44
	PN 10 mg	28	11.4	5.41	0.89	3.90	1.36*	3.16	34	11.4	4.97	1.24*	3.10
	PN 15 mg	35	13.7	5.17	0.[illegible]	4.02	0.29	3.76	40	13.6	4.86	0.63	4.02
	PN 20 mg	32	12.8	3.78	1.44(*)	4.17	1.19(*)	3.93	39	12.[illegible]	3.66	1.15(*)	3.70
	Placebo	31	12.4	3.77	0.07	3.01	-0.55	2.41	36	12.8	4.32	0.35	2.81

(+)p<0.10, *p<.05, **p<.01, ***p<.001

(22.0.2315)

TABLE 33 (Continued)

PN 200-110 STUDY NO. 304

SUMMARY OF LAB RESULTS
FOR CHEMISTRY DATA

Test (Normal Range)	Treatment Group	Completers Only							All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change	S.D.	Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
Alkaline Phosphatase IU/L (10-45)	PN 5 mg	33	26.3	7.88	3.00**	5.91	1.27	6.19	37	26.6	7.69	1.30	6.12
	PN 10 mg	29	25.7	6.97	1.69(*)	4.79	5.62**	8.76	35	25.9	7.12	5.86***	8.00
	PN 15 mg	39	28.8	9.70	0.26 (δ)	5.89	1.03	5.87	41	29.2	9.71	0.98	5.74
	PN 20 mg	36	28.3	.71	2.47*	5.97	1.69 (δ)	4.91	41	28.0	7.46	1.10	5.01
	Placebo	34	29.6	6.15	-1.00	7.01	-1.15	4.65	39	29.4	8.39	-0.64	4.57
LDH IU/L (120-250)	PN 5 mg	31	168.9	35.31	-0.61	20.29	0.65	36.23	36	169.4	34.36	0.28	33.71
	PN 10 mg	28	168.4	28.90	-2.85 (†)	24.83	6.96	68.28	34	169.3	29.93	5.29	60.46
	PN 15 mg	37	177.9	25.85	2.76	20.18	0.54	22.30	39	178.8	26.26	0.74	21.78
	PN 20 mg	36	177.7	44.06	8.22	31.26	0.06	24.64	41	172.6	42.20	0.58	23.76
	Placebo	31	165.9	30.16	8.23*	17.05	2.39	20.58	37	165.1	27.88	4.21	21.01
SGOT IU/L (10-50,	PN 5 mg	33	27.4	10.88	3.67 (δ)	14.35	2.06	11.73	37	28.0	10.77	2.91 (δ)	11.50
	PN 10 mg	29	25.7	9.42	2.35	8.02	0.72	9.51	35	26.9	9.53	3.53	20.55
	PN 15 mg	39	24.7	7.03	2.49	13.64	-0.08	7.24	41	24.7	6.86	-0.10	7.10
	PN 20 mg	36	25.4	8.58	2.81*	8.01	-0.25	9.99	41	25.6	8.14	-0.32	9.63
	Placebo	34	29.5	13.71	-0.94	9.70	-2.91(*)	8.42	39	28.5	13.26	-2.13	8.24

(*)p<0.10, *p<.05, **p<.01, ***p<.001

TABLE 33 (Continued)

PN 2.0-1:0 STUDY NO. 201

SUMMARY COMPARATIVE RESULTS
FOR CHEMISTRY DATA

Variable (Normal Range)	Treatment Group	Completers Only							All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change		Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
SGPT IU/L (5-55)	PN 5 mg	33	23.1	14.63	1.49	10.46	1.18	7.78	37	23.6	14.56	1.49	7.70
	PN 10 mg	29	20.8	9.05	2.45	10.51	1.31	8.60	35	23.8	12.34	1.29	9.45
	PN 15 mg	39	22.3	11.84	3.13	17.64	1.44	6.24	41	22.3	11.54	1.46	6.09
	PN 20 mg	36	21.5	12.57	1.50	9.58	-1.67	10.32	41	24.5	12.36	-0.81	10.53
	Placebo	33	34.1	23.49	-2.00	13.23	-3.67	12.67	38	29.3	22.54	-2.68	12.10
Sodium mEq/l (134-143)	PN 5 mg	32	139.1	2.10	0.00	2.23	-0.50	2.51	37	139.0	2.06	-0.38	2.71
	PN 10 mg	28	139.3	1.90	-0.64	3.22	-0.25	2.12	34	139.1	2.01	0.03	2.21
	PN 15 mg	35	138.9	2.33	0.00	3.18	-0.31	2.87	40	138.9	2.24	-0.28	2.82
	PN 20 mg	32	138.5	2.46	-0.44	2.66	-0.31	2.79	39	138.7	2.28	-0.36	2.75
	Placebo	31	139.2	2.25	-0.61	2.64	0.26	2.50	36	139.4	2.36	0.31	2.52
Potassium mEq/l (3.5-5.3)	PN 5 mg	32	4.14	0.35	0.02	0.31	0.03	0.30	37	4.14	0.34	0.01	0.31
	PN 10 mg	28	4.13	0.46	-0.21**	0.36	-0.02	0.49	34	4.16	0.43	-0.04	0.45
	PN 15 mg	35	4.29	0.39	-0.20**	0.37	-0.20***	0.37	40	4.29	0.44	-0.21**	0.39
	PN 20 mg	32	4.35	0.56	-0.15(*)	0.45	-0.16(*)	0.47	35	4.32	0.51	-0.13(*)	0.45
	Placebo	31	4.17	0.36	0.03	0.33	0.01	0.36	36	4.13	0.41	0.00	0.34

(*)p<0.10, *p<.05, **p<.01, ***p<.001

TABLE 33 (Continued)

PN 220-[illegible] STUDY [illegible] 201

SUMMARY COMPARATIVE RESULTS
FCT CHEMISTRY DATA

Test (Normal Range)	Treatment Group	Completers Only							All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change	S.D.	Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
Albumin gm% (3.7-5.0)	PN 5 mg	32	4.14	0.37	0.11*	0.24	0.03	0.26	37	4.17	0.35	0.04	0.25
	PN 10 mg	28	4.06	0.24	0.09*	0.21	0.13**	0.23	34	4.09	0.29	0.14***	0.21
	PN 15 mg	35	4.10	0.26	0.11*	0.24	0.09*	0.23	40	4.12	0.27	0.08*	0.22
	PN 20 mg	32	4.16	0.25	0.08(*)	0.25	0.04	0.30	39	4.17	0.31	0.04	0.31
	Placebo	30	4.09	0.30	0.09(*)	0.25	[illegible]	0.28	35	4.09	0.29	0.06	0.28
Total Bilirubin mg/dl (0.2-1.6)	PN 5 mg	33	0.56	[illegible].25	0.05	0.22	-0.01	0.23	37	0.56	0.24	0.00	0.22
	PN 10 mg	29	0.59	0.27	-0.06	0.20	-0.04	0.27	35	0.60	0.28	-0.01	0.27
	PN 15 mg	39	0.54	0.19	0.00	0.17	-0.05(*)	0.18	41	0.55	0.19	-0.06*	0.17
	PN 20 mg	36	0.52	0.23	0.02	0.22	-0.02	0.21	41	0.51	0.22	-0.03	0.21
	Placebo	33	0.51	0.19	0.02	0.13	0.01	0.14	38	0.50	0.18	0.02	0.15
Cholesterol mg/dl (120-290)	PN 5 mg	32	215.4	45.75	-0.03	22.72	0.78	20.35	37	217.7	45.92	2.03	19.61
	PN 10 mg	28	220.2	43.33	5.39(*)	15.56	7.32	23.21	34	220.6	42.74	7.59(*)	22.77
	PN 15 mg	35	208.0	36.44	3.23	16.84	1.40	22.95	40	205.2	36.27	1.15	21.65
	PN 20 mg	32	209.4	42.36	5.66	20.33	-0.03	23.07	39	211.2	40.24	0.26	23.72
	Placebo	31	210.7	34.65	6.10	22.62	-0.42	17.56	36	211.8	34.91	2.53	19.73

(*)p<0.10, *p<.05, **p<.01, ***p<.001

TABLE 33(CONT.)

07-02-[illegible]

TABLE 33 (Continued)

PD 220-10 STUDY NO. 301

SUMMARY COMPARATIVE RESULTS
FOR CHEMISTRY DATA

Variable (Normal Range)	Treatment Group	Completers Only							All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change	S.D.	Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
Uric Acid mg/dl (2.2-8.3)	PN 5 mg	32	5.93	1.22	-0.12	0.65	-0.10	0.58	37	5.86	1.22	-0.03	0.62
	PN 10 mg	28	5.61	1.36	0.13	1.15	0.33*	0.73	34	5.56	1.27	0.35**	0.71
	PN 15 mg	35	5.53	1.55	0.20	1.03	0.15	1.06	40	5.87	1.60	0.10	1.02
	PN 20 mg	32	5.77	1.40	0.07	0.94	-0.15	0.91	39	5.75	1.37	-0.13	0.85
	Placebo	30	5.66	1.09	0.25*	0.62	0.05	0.74	35	5.63	1.08	0.09	0.73
Glucose mg/dl (65-130)	PN 5 mg	32	104.9	26.68	8.22	20.61	1.66	24.18	37	106.4	26.45	1.22	25.36
	PN 10 mg	28	104.8	20.92	7.14	24.57	5.61	22.28	34	102.3	20.07	6.65	29.82
	PN 15 mg	35	104.1	29.38	1.89	20.25	1.60	14.83	40	103.2	27.63	1.80	14.40
	PN 20 mg	32	110.5	38.68	5.81	21.18	0.13	21.18	39	108.8	35.51	-0.33	19.81
	Placebo	31	106.7	31.94	7.00(*)	22.66	2.74	25.06	36	106.6	31.06	2.64	28.03
Total Protein gm/dl (6.4-8.1)	PN 5 mg	32	7.19	0.37	0.16*	0.35	0.06	0.36	37	7.20	0.35	0.04	0.34
	PN 10 mg	28	7.20	0.35	0.13*	0.34	0.16(*)	0.45	34	7.22	0.37	0.17*	0.47
	PN 15 mg	35	7.32	0.59	0.09	0.32	0.04	0.39	40	7.31	0.57	0.04	0.38
	PN 20 mg	32	7.21	0.39	0.12*	0.31	0.06	0.35	39	7.23	0.39	0.03	0.33
	Placebo	31	7.10	0.41	0.07	0.32	0.04	0.47	36	7.12	0.42	0.02	0.44

(*)p<0.10, *p<.05, **p<.01, ***p<.001

TABLE 33 (Continued)

PN 120-110 STUDY NO. 301

SUMMARY COMPARATIVE RESULTS
FOR CHEMISTRY DATA

Variable (Normal Range)	Treatment Group	Completers Only							All Patients				
		No. of Patients	Baseline		Week 3		Week 5		No. of Patients	Baseline		Endpoint	
			Mean	S.D.	Mean Change	S.D.	Mean Change	S.D.		Mean	S.D.	Mean Change	S.D.
Chloride mEq/l (96-107)	PN 5 mg	32	102.1	3.16	0.13	4.11	-0.47	3.35	37	102.0	3.16	-0.30	3.28
	PN 10 mg	28	102.1	3.09	0.75	3.37	0.64	3.64	34	102.2	3.12	0.59	3.46
	PN 15 mg	35	101.5	2.54	-0.43	2.86	-0.37	2.93	40	103.6	2.53	-0.58	3.00
	PN 20 mg	32	103.3	2.92	-0.03	2....	-1.13(*)	3.35	39	103.3	2.73	-1.2**	3.15
	Placebo	31	102.4	2.39	0.19	3.25	0.19	4.54	36	102.7	2.85	0.00	4.41
CO_2 mEq/l (25-32)	PN 5 mg	31	26.2	2.97	0.05	2.47	0.27	2.47	37	26.2	2.85	-0.04	2.44
	PN 10 mg	28	26.1	3.08	-0.70	3.20	-0.52	2.65	34	26.0	2.85	-0.29	2.53
	PN 15 mg	33	25.3	3.02	0.11	3.26	-0.33	3.28	**	25.5	3.08	-0.11	3.16
	PN 20 mg	29	25.3	2.60	-0.05	3.05	0.78	3.61	38	25.3	2.65	1.07(*)	3.57
	Placebo	29	26.7	2.54	-0.48	2.99	-0.07	3.09	34	26.7	2.50	-0.01	2.88
Creatinine mg/dl (0.6-1.3)	PN 5 mg	32	1.06	0.21	0.01	0.12	0.03	0.18	37	1.06	0.20	0.02	0.20
	PN 10 mg	28	0.97	0.18	0.03	0.13	0.05	0.17	34	0.99	0.17	0.06(*)	0.17
	PN 15 mg	35	1.11	0.31	0.01	0.22	0.01	0.26	40	1.10	0.29	0.02	0.27
	PN 20 mg	32	1.05	0.17	-0.01	0.17	0.01	0.17	39	1.04	0.16	0.01	0.17
	Placebo	30	1.09	0.21	0.00	0.15	-0.01	0.16	35	1.08	0.20	-0.02	0.17

(*)p<0.10, *p<.05, **p<.01, ***p<.001

(4)

TABLE 33(CONT.)

TABLE 34
.. 200-110 STUDY NO. 251

LABORATORY DATA - HEMATOLOGY
RECURRING LABORATORY ABNORMALITIES

Treatment Group	Patient No.	Variable (Normal Range)	Initial Visit	Placebo Washout		Active Treatment††				Abnormal High (H) or Abnormal Low (L)
				Week -2	Baseline (Week -1)	Week 1	Week 3	Week 4	Week 5	
PN 200-110 10 mg	610	Bands % (0-5)			4			0	8	H
	617	Eosinophils % (0-8)	3		6		10		7	H
15 mg	467	Monocytes % (0-10)	7		8				12	H
	508	Eosinophils % (0-8)	6		8		8		12	H
	512	Basophils % (0-2)	2		1		1		3	H
20 mg	469	Lymphocytes % (10-47)	45		24		60		45	H
	504	Basophils % (0-2)	1		0		3		3	H
	615	Basophils % (0-2)	1		2		0		3	H
Placebo	204	Monocytes % (0-10)	0		10		12			H
	503	Neutrophils % (42-81)	58		51		33			L
	503	Eosinophils % (0-8)	5		5		12			H
	510	Neutrophils % (42-81)	42		42	43	33		38	L
	510	Lymphocytes % (10-47)	52		45	52	60		52	H
	614	WBC x 10^3 cu mm (3.9-11.4)	3.6	4.3	3.4		3.2	3.7	3.5	L

†Defined as all pre-dose evaluations being normal and at least one abnormal post-dose evaluation based on adjusted normal limits or an abnormal baseline value that worsened by at least 15%.

††Underlined laboratory values indicate an abnormality.

LABORATORY DATA - CHEMISTRY
NEWLY-OCCURRING LABORATORY ABNORMALITIES†

Treatment Group	Patient No.	Variable (Normal Range)	Initial Visit††	Wk -2	Baseline (Wk -1)††	Active Treatments††							Abnormal High (H) or Abnormal Low (L)
						Wk 1	Wk 2	Wk 3	Follow-up	Wk 4	Wk 5	Follow-up	
PN 200-110 5 mg	203	LDH u/L (110-250)	187		171			199			329		H
	212	SGOT u/L (10-50)	41		38	37		111*		31	37	35	H
	326	Creatinine mg/dl (0.6-1.3)	1.0		1.3			1.3			1.7		H
	354	Glucose mg/dl (65-130)	128		98			158*			116		H
	354	Alkaline Phos. u/L (10-45)	31		34	52*	32	45		39	40		H
	354	SGOT u/L (10-50)	61*		47	75*	47	63*		54*	55*		H†††
	354	SGPT u/L (5-55)	50		53	68*	40	53		54	48		H
	357	Creatinine mg/dl (0.6-1.3)			1.2			1.7*			1.3		H
	405	Glucose mg/dl (65-130)	236*		210*			308*			267*		H†††
	460	Glucose mg/dl (65-130)	126		126			165*					H
	460	Creatinine mg/dl (0.6-1.3)	1.4		1.3			1.6*					H
	463	SGOT u/L (10-50)	46		50			49			90		H
	463	SGPT u/L (5-55)	42		45			48			68		H
	504	SGPT u/L (5-55)	70		62	81	51	58		80	46	30	H†††
	554	Glucose mg/dl (65-130)	132		133			180			124		H
	618	SGOT u/L (10-50)	40		44	40	38	36		65	40		H
	659	Alkaline Phos. u/L (10-45)	41		45	54	53	48		52	42		H
	659	SGPT u/L (5-55)	56		60	66	66	68		64	64		H

†Defined as all pre-dose evaluations being normal and at least one abnormal post-dose evaluation based on adjusted normal limits or an abnormal baseline value that worsened by at least 15%.
††Underlined laboratory values indicate an abnormality.
†††Abnormal at baseline and worsening by at least 15%.

Note: Asterisks indicate clinically significant laboratory abnormalities noted by the investigator.

T... 57 (...inued)
PN 200-110 STUDY NO. 301

LABORATORY DATA - CHEMISTRY
NEWLY-OCCURRING LABORATORY ABNORMALITIES†

Treatment Group	Patient No.	Variable (Normal Range)	Initial Visit††	Wk -2	Baseline (Wk -1)††	Active Treatments††							Abnormal High (H) or Abnormal Low (L)
						Wk 1	Wk 2	Wk 3	Follow-up	Wk 4	Wk 5	Follow-up	
PN 200-110 10 mg	155	Glucose mg/dl (65-130)	224*		166			267*			281*	319*	H†††
	255	Alkaline Phos. u/L (10-45)	50	43	46	32	29	41		45	53	41	H
	312	Glucose mg/dl (65-130)	94		85			157			106		H
	313	SGPT u/L (5-55)	23		45			75*			49		H
	313	Potassium mEq/l (3.5-5.3)	3.6		3.5			2.9*			3.3		L
	324	Uric Acid mg/dl (2.2-8.3)	6.0		8.2			7.6			9.7		H
	411	SGOT u/L (10-50)	48		38	39		147*	37				H
	455	Glucose mg/dl (65-130)	116		112			115			186		H
	509	Alkaline Phos. u/L (10-45)	38		28	33	39	39		39	52		H
	513	Glucose mg/dl (65-130)	154			182		158		178	226		H†††
	601	LDH u/L (110-250)	158		107			159			513*		H
	610	Cholesterol mg/dl (120-290)	279		287					342	323		H

†Defined as all pre-dose evaluations being normal and at least one abnormal post-dose evaluation based on adjusted normal limits or an abnormal baseline value that worsened by at least 15%.
††Underlined laboratory values indicate an abnormality.
†††Abnormal at baseline and worsening by at least 15%.

Note: Asterisks indicate clinically significant laboratory abnormalities noted by the investigator.

TABLE 37 (Continued)
PN 200-110 STUDY NO. 301

LABORATORY DATA - CHEMISTRY
NEWLY-OCCURRING LABORATORY ABNORMALITIES†

Treatment Group	Patient No.	Variable (Normal Range)	Initial Visit	Wk -3	Baseline (Wk -1)	Active Treatments††									Abnormal High (H) or Abnormal Low (L)
						Wk 1	Wk 2	Follow-up*							
PN 200-110 10 mg (cont'd)	611	Total Bilirubin mg/dl (0.2-1.6)	1.7	1.1	1.3	4.0*	1.6	3.2*	1.7	1.4	1.8	1.5	1.3	1.1	H
	611	LDH u/L (110-250)	170	219	186	1213*	204	193	181	185	208	108	183	165	H
	611	SGOT u/L (10-50)	39	31	34	101*	38	34	30	27	33	30	35	60*	H
	611	SGPT u/L (5-55)	61*	52	38	43	45	44	35	44	33	49	41	128*	H

†Defined as all pre-dose evaluations being normal and at least one abnormal post-dose evaluation based on adjusted normal limits or an abnormal baseline value that worsened by least 15%.
††Underlined laboratory values indicate an abnormality.

*The duration of follow-up visits was approximately six weeks.

Note: Asterisks indicate clinically significant laboratory abnormalities noted by the investigator.

LABORATORY DATA - CHEMISTRY
FREQUENTLY-OCCURRING LABORATORY ABNORMALITIES

Treatment Group	Patient No.	Variable (Normal Range)	Initial Visit††	Wk -2	Baseline (Wk -1)††	Active Treatments††							Abnormal High (H) or Abnormal Low (L)
						Wk 1	Wk 2	Wk 3	Follow-up	Wk 4	Wk 5	Follow-up	
PN 200-110 15 mg	110	Creatinine mg/dl (0.6-1.3)	1.6		1.8	1.6		2.1			1.8		H†††
	159	Alkaline Phos. u/L (10-45)	46		56	65	69	59		63	60	56	H†††
	215	Uric Acid mg/dl (2.2-8.3)	7.1		5.7			10.2			9.2		H
	224	Alkaline Phos. u/L (10-45)	24		29	36	55	27		36	35	28	H
	254	SGOT u/L (10-50)	43		34			106*		39	36	37	H
	254	SGPT u/L (5-55)	58		58			161*		73	35	52	H
	309	Creatinine mg/dl (0.6-1.3)	1.5		1.5			1.6*			2.8*		H
	317	BUN mg/dl (6-23)	12		18			29			27		H
	317	Creatinine mg/dl (0.6-1.3)	1.2		1.5			1.8			1.5		H
	322	Glucose mg/dl (65-130)	151*		162*			226*			161*		H†††
	322	SGPT u/L (5-55)	62		54	62	59	59		59	65		H
	361	Alkaline Phos. u/L (10-45)	23		29	59		31		42	31		H
	415	BUN mg/dl (6-23)	26		26		21	15			27		H
	415	LDH u/L (110-250)	163		164	150	150	179		294	143		H
20 mg	214	LDH u/L (110-250)	200		166	216	197	321		197	219	198	H
	320	Glucose mg/dl (65-130)	111		114			162			97		H
	320	SGPT u/L (5-55)	22		11	11	112*	28		13	14		H

†Defined as all pre-dose evaluations being normal and at least one abnormal post-dose evaluation based on adjusted normal limits or an abnormal baseline value that worsened by least 15%.
††Underlined laboratory values indicate an abnormality.
†††Abnormal at baseline and worsening by at least 15%.
Note: Asterisks indicate clinically significant laboratory abnormalities noted by the investigator.

TABLE 37 (CONTD)

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LABORATORY DATA - CHEMISTRY
NEWLY-OCCURRING LABORATORY ABNORMALITIES†

Treatment Group	Patient No.	Variable (Normal Range)	Initial Visit†	Wk -2	Baseline (Wk -1)††	Active Treatments†††							Abnormal High (H) or Abnormal Low (L)
						Wk 1	Wk 2	Wk 3	Follow-up	Wk 4	Wk 5	Follow-up	
Placebo	109	Cholesterol mg/dl (120-290)	301		276			338					H
	117	Alkaline Phos. u/L (10-45)	44		39			27			40	55	H
	161	Cholesterol mg/dl (120-290)			277			350			309		H
	251	Inorganic Phosphorus mg/dl (2.2-4.6)	2.5		2.6			1.8			2.8		L
	304	Glucose mg/dl (65-130)	140		149			166			95		H
	413	Glucose mg/dl (65-130)	133					134			166		H
	421	Alkaline Phos. u/L (10-45)	30		42	27	44	33		41	35		H
	453	Glucose mg/dl (65-130)			93	104		153			124		H
	510	Alkaline Phos. u/L (10-45)	40		45	60	48	46			51	58	H
	556	Alkaline Phos. u/L (10-45)	48		50	54	53	53		40	42	48	H
	619	Glucose mg/dl (65-130)	127			234*		107			114		H
	656	SGPT u/L (5-55)	54		50	43	64	64		45	56		H

†Defined as all pre-dose evaluations being normal and at least one abnormal post-dose evaluation based on adjusted normal limits or an abnormal baseline value that worsened by least 15%.
††Underlined laboratory values indicate an abnormality.
†††Abnormal at baseline and worsening by at least 15%.

Note: Asterisks indicate clinically significant laboratory abnormalities noted by the investigator.

TABLE 37 (CONTD

TABLE 39
PN 200-110 STUDY NO. 301

SUMMARY OF ECHOCARDIOGRAPHIC DATA
CENTER A ONLY
COMPLETED PATIENTS ONLY

Variable*	Treatment Group	No. of Patients	Baseline		Mean Change	S.D.
			Mean	S.D.		
Left Ventricular Internal Diameter Diastole (mm)	PN 5 mg	5	43.00	6.00	1.40	2.51
	PN 10 mg	1	44.00	-	6.00	-
	PN 15 mg	5	49.60	7.02	1.00 (•)	2.83
	PN 20 mg	3	51.33	2.52	-1.00	1.00
	Placebo	5	45.20	4.82	0.40	2.70
Left Ventricular Internal Diameter Systole (mm)	PN 5 mg	5	25.20	8.17	-0.20	5.72
	PN 10 mg	1	30.00	-	2.00	-
	PN 15 mg	5	34.00	9.92	-0.20	2.77
	PN 20 mg	3	33.33	2.52	-1.33	2.52
	Placebo	5	29.40	4.56	-0.80	2.59
Septal Wall Thickness (mm)	PN 5 mg	5	10.60	2.41	-0.60	0.89
	PN 10 mg	1	13.00	-	-1.00	-
	PN 15 mg	5	11.40	0.55	-0.40	1.82
	PN 20 mg	3	8.67	1.15	1.67	1.53
	Placebo	5	10.40	2.07	1.00	2.55
Posterior Wall Thickness (mm)	PN 5 mg	5	10.60	2.41	-0.20	1.64
	PN 10 mg	1	12.00	-	-1.00	-
	PN 15 mg	5	11.80	1.30	-0.80(•)	0.84
	PN 20 mg	3	9.33	1.15	0.33	0.58
	Placebo	5	10.40	0.89	0.40	0.89
Left Atrial Diameter Systole (mm)	PN 5 mg	5	37.80	1.48	-0.20	6.83
	PN 10 mg	3	42.00	3.61	-2.33	7.57
	PN 15 mg	6	37.00	2.53	1.17	6.91
	PN 20 mg	3	40.33	3.51	0.67	4.73
	Placebo	5	42.20	3.42	-1.20	2.28

(•)p<.10, •p<.05, ••p<.01, •••p<.001
*Each variable is the mean of 3 measurements.

TABLE 39 (CONTINUED)
PN 200-110 STUDY NO. 301

SUMMARY OF ECHOCARDIOGRAPHIC DATA
CENTER A ONLY
COMPLETED PATIENTS ONLY

Variable	Treatment Group	No. of Patients	Baseline		Mean Change	S.D.
			Mean	S.D.		
End Diastolic Volume (ml)	PN 5 mg	5	85.00	31.75	5.40	13.28
	PN 10 mg	1	88.00	-	34.00	-
	PN 15 mg	5	118.60	42.90	9.60	20.95
	PN 20 mg	3	126.00	16.52	-6.33	7.77
	Placebo	5	96.20	24.25	0.80	16.45
End Diastolic Volume Index (ml/M^2)	PN 5 mg	5	47.80	14.67	1.60	9.15
	PN 10 mg	1	44.00	-	17.00	-
	PN 15 mg	5	64.60	17.79	4.80	10.76
	PN 20 mg	3	67.00	5.00	-1.67	4.04
	Placebo	5	52.60	13.39	0.40	8.11
End Systolic Volume (ml)	PN 5 mg	5	26.00	20.43	-3.00	15.38
	PN 10 mg	1	34.00	-	6.00	-
	PN 15 mg	5	53.40	39.22	1.60	12.60
	PN 20 mg	3	45.67	7.02	-7.00(*)	3.61
	Placebo	5	34.00	12.21	-1.20	6.72
End Systolic Volume Index (ml/M^2)	PN 5 mg	5	14.20	9.91	-1.80	7.73
	PN 10 mg	1	17.00	-	3.00	-
	PN 15 mg	5	28.40	17.98	0.80	5.42
	PN 20 mg	3	24.00	1.73	-3.33(*)	1.53
	Placebo	5	15.00	10.65	3.20	8.29

+p<.10, *p<.05, **p<.01, ***p<.001

TABLE 39 (CONTINUED)
PN 200-110 STUDY NO. 301

SUMMARY OF ECHOCARDIOGRAPHIC DATA
CENTER A ONLY
COMPLETED PATIENTS ONLY

Variable	Treatment Group	No. of Patients	Baseline		Mean Change	S.D.
			Mean	S.D.		
Stroke Volume (ml)	PN 5 mg	5	58.80	13.85	6.00	15.12
	PN 10 mg	1	54.00	-	27.00	-
	PN 15 mg	5	65.80	11.58	7.40	9.07
	PN 20 mg	3	82.00	13.23	1.00	4.58
	Placebo	5	62.00	16.99	2.00	13.04
Cardiac Output (L/min)	PN 5 mg	5	4.52	1.01	0.65	0.99
	PN 10 mg	1	3.97	-	2.78	-
	PN 15 mg	5	3.86	0.27	0.55	0.60
	PN 20 mg	3	6.19	2.31	-0.10	1.11
	Placebo	5	4.34	0.96	0.01	0.98
Cardiac Index ($L/min/M^2$)	PN 5 mg	5	2.58	0.51	0.22	0.59
	PN 10 mg	1	2.00	-	1.36	-
	PN 15 mg	5	2.16	0.29	0.28	0.34
	PN 20 mg	3	3.22	1.01	-0.01	0.59
	Placebo	5	2.37	0.46	0.01	0.53
Ejection Fraction %	PN 5 mg	5	71.66	12.86	1.70	10.58
	PN 10 mg	1	61.40	-	5.50	-
	PN 15 mg	5	58.68	14.83	3.22(*)	2.02
	PN 20 mg	3	64.17	4.64	3.73**	0.47
	Placebo	5	64.80	8.06	2.04	5.90

(*)p<.10, *p<.05, **p<.01, ***p<.001

TABLE 39 (CONTINUED)
PN 200-110 STUDY NO. 301

SUMMARY OF ECHOCARDIOGRAPHIC DATA
CENTER A ONLY
COMPLETED PATIENTS ONLY

Variable	Treatment Group	No. of Patients	Baseline		Mean Change	S.D.
			Mean	S.D.		
Mean Velocity Circumferential Shortening	PN 5 mg	5	1.52	0.49	-0.05	0.54
	PN 10 mg	1	0.99	-	0.63	-
	PN 15 mg	5	1.00	0.35	0.07 (*)	0.11
	PN 20 mg	3	1.22	0.36	0.05	0.23
	Placebo	5	1.2[illegible]	0.35	-0.06	0.17
Left Ventricular Mass (gm)	PN 5 mg	5	181.40	70.47	0.20	30.96
	PN 10 mg	1	252.00	-	6.00	-
	PN 15 mg	5	259.40	61.34	-7.20	34.67
	PN 20 mg	3	197.00	52.57	18.67	28.43
	Placebo	5	195.20	67.50	19.20	43.37
Left Ventricular Mass Index (gm/M^2)	PN 5 mg	5	105.00	48.52	-5.40	24.71
	PN 10 mg	1	126.00	-	2.00	-
	PN 15 mg	5	142.00	18.72	-4.00	22.49
	PN 20 mg	3	104.00	28.62	10.67	14.36
	Placebo	5	106.60	32.88	10.60	23.12
Relative Wall Thickness	PN 5 mg	5	0.50	0.13	-0.03	0.10
	PN 10 mg	1	0.56	-	-0.13	-
	PN 15 mg	5	0.48	0.08	-0.04 (*)	0.05
	PN 20 mg	3	0.36	0.05	0.02	0.04
	Placebo	5	0.46	0.03	0.02	0.05

p<.10, *p<.05, **p<.01, ***p<.001

TABLE 39 (CONTINUED)
PN 200-110 STUDY NO. 301

SUMMARY OF ECHOCARDIOGRAPHIC DATA
CENTER A ONLY
COMPLETED PATIENTS ONLY

Variable	Treatment Group	No. of Patients	Baseline		Mean Change	S.D.
			Mean	S.D.		
Body Surface Area (M^2)	PN 5 mg	5	1.76	0.18	0.07	0.09
	PN 10 mg	3	2.01	0.02	-0.01	0.02
	PN 15 mg	6	1.90	0.29	0.01 (*)	0.03
	PN 20 mg	3	1.90	0.22	-0.02	0.02
	Placebo	5	1.82	0.12	0.02	0.03
Heart Rate (beats/min)	PN 5 mg	5	77.60	6.77	0.00	9.49
	PN 10 mg	3	66.33	12.42	11.33	7.77
	PN 15 mg	6	59.67	10.07	3.50	5.09
	PN 20 mg	3	73.67	17.24	0.00	14.57
	Placebo	5	71.00	10.51	-3.00	4.30
Left Atrial Index (cm/M^2)	PN 5 mg	5	2.16	0.18	-0.12	0.28
	PN 10 mg	3	2.13	0.15	-0.13	0.32
	PN 15 mg	6	2.00	0.30	0.00	0.34
	PN 20 mg	3	2.17	0.31	0.00	0.27
	Placebo	5	2.32	0.23	-0.08	0.15
Fractional Shortening %	PN 5 mg	5	42.26	12.22	0.78	9.09
	PN 10 mg	1	32.70	-	4.20	-
	PN 15 mg	5	30.74	8.97	3.18*	1.38
	PN 20 mg	3	34.90	3.54	2.93**	0.25
	Placebo	5	35.54	6.20	1.78	4.68

(*)p<.10, *p<.05, **p<.01, ***p<.001

TABLE 39 (CONTINUED)
PN 200-110 STUDY NO. 301

SUMMARY OF ECHOCARDIOGRAPHIC DATA
CENTER A ONLY
COMPLETED PATIENTS ONLY

Variable	Treatment Group	No. of Patients	Baseline		Mean Change	S.D.
			Mean	S.D.		
Peak Eno Systolic Stress ($dynes/cm^2$)	PN 5 mg	5	99.22	60.99	-3.52	36.93
	PN 10 mg	1	76.60	-	29.30	-
	PN 15 mg	5	108.18	25.38	8.42	55.84
	PN 20 mg	3	144.63	9.08	-13.57(*)	5.76
	Placebo	5	106.66	24.91	-11.26	28.65

(*)p<.10, *p<.05, **p<.01, ***p<.001

TABLE 44
CN 200-110 STUDY NO. 301
SUMMARY OF 24 HOUR AMBULATORY BLOOD PRESSURE MONITOR

VARIABLE	LABEL	N*	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE
PATIENT NUMBER=109	TREATMENT CODE=PLACEBO	WEEK NUMBER=-1				
SYS	SYSTOLIC PRESSURE MMHG	55	117.81818182	13.07965753	94.00000000	161.00000000
DIAS	DIASTOLIC PRESSURE MMHG	55	84.92727273	8.76552959	79.00000000	109.00000000
HRTRATE	HEART RATE BEATS/MIN.	55	68.72727273	14.91141068	48.00000000	150.00000000
PATIENT NUMBER=109	TREATMENT CODE=PLACEBO	WEEK NUMBER=3				
SYS	SYSTOLIC PRESSURE MMHG	48	135.91666667	17.20691763	91.00000000	172.00000000
DIAS	DIASTOLIC PRESSURE MMHG	48	103.77083333	8.80065040	72.00000000	120.00000000
HRTRATE	HEART RATE BEATS/MIN.	48	90.58333333	21.85136768	63.00000000	179.00000000
PATIENT NUMBER=111	TREATMENT CODE=10 MG	WEEK NUMBER=-1				
SYS	SYSTOLIC PRESSURE MMHG	71	137.22535211	21.54478879	99.00000000	228.00000000
DIAS	DIASTOLIC PRESSURE MMHG	71	101.04225352	13.91960244	78.00000000	134.00000000
HRTRATE	HEART RATE BEATS/MIN.	71	84.85774648	11.05755930	66.00000000	120.00000000
PATIENT NUMBER=11.	TREATMENT CODE=10 MG	WEEK NUMBER=5				
SYS	SYSTOLIC PRESSURE MMHG	75	142.26666667	16.63709088	99.00000000	179.00000000
DIAS	DIASTOLIC PRESSURE MMHG	75	105.22666667	13.49832155	69.00000000	141.00000000
HRTRATE	HEART RATE BEATS/MIN.	75	82.78000000	13.03720249	62.00000000	119.00000000
PATIENT NUMBER=113	TREATMENT CODE=PLACEBO	WEEK NUMBER=-4				
SYS	SYSTOLIC PRESSURE MMHG	143	128.86433566	15.89930841	80.00000000	168.00000000
DIAS	DIASTOLIC PRESSURE MMHG	143	93.46853147	11.24365498	58.00000000	128.00000000
HRTRATE	HEART RATE BEATS/MIN.	143	94.13986014	9.19552968	75.00000000	127.00000000
PATIENT NUMBER=113	TREATMENT CODE=PLACEBO	WEEK NUMBER=4				
SYS	SYSTOLIC PRESSURE MMHG	108	137.24074074	23.39337328	107.00000000	253.00000000
DIAS	DIASTOLIC PRESSURE MMHG	108	87.06481481	14.84367815	59.00000000	134.00000000
HRTRATE	HEART RATE BEATS/MIN.	108	96.60185185	18.03005788	65.00000000	159.00000000
PATIENT NUMBER=114	TREATMENT CODE=20 MG	WEEK NUMBER=-3				
SYS	SYSTOLIC PRESSURE MMHG	186	139.39247312	19.28482802	99.00000000	188.00000000
DIAS	DIASTOLIC PRESSURE MMHG	186	89.05913978	12.89675204	65.00000000	119.00000000
HRTRATE	HEART RATE BEATS/MIN.	186	74.64516129	8.02111425	59.00000000	102.00000000
PATIENT NUMBER=114	TREATMENT CODE=20 MG	WEEK NUMBER=4				
SYS	SYSTOLIC PRESSURE MMHG	187	127.19786096	18.07902062	78.00000000	181.00000000
DIAS	DIASTOLIC PRESSURE MMHG	187	79.04224599	12.32492366	54.00000000	127.00000000
HRTRATE	HEART RATE BEATS/MIN.	187	72.28342246	10.45213839	57.00000000	110.00000000

* REPRESENTS THE NUMBER OF READINGS TAKEN DURING EACH RECORDING PERIOD.

TABLE 44
[illegible] STUDY NO. 301
SUMMARY OF 24 HOUR AMBULATORY BLOOD PRESSURE MONITOR

VARIABLE	LABEL	N *	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE
---------- PATIENT NUMBER=115 TREATMENT CODE=5 MG WEEK NUMBER=-2 ----------						
SYS	SYSTOLIC PRESSURE MMHG	101	133.47120419	21.15451820	72.00000000	176.00000000
DIAS	DIASTOLIC PRESSURE MMHG	101	73.97382199	13.74751061	50.00000000	117.00000000
HRTRATE	HEART RATE BEATS/MIN.	101	72.47643979	8.04318737	54.00000000	96.00000000
---------- PATIENT NUMBER=115 TREATMENT CODE=5 MG WEEK NUMBER=5 ----------						
SYS	SYSTOLIC PRESSURE MMHG	112	111.41964286	27.11724241	72.00000000	249.00000000
DIAS	DIASTOLIC PRESSURE MMHG	112	82.05357143	16.54251377	52.00000000	124.00000000
HRTRATE	HEART RATE BEATS/MIN.	112	84.42857143	28.04877164	59.00000000	203.00000000
---------- PATIENT NUMBER=116 TREATMENT CODE=15 MG WEEK NUMBER=-2 ----------						
SYS	SYSTOLIC PRESSURE MMHG	75	133.45333333	17.55015464	90.00000000	181.00000000
DIAS	DIASTOLIC PRESSURE MMHG	75	101.40000000	18.43508852	64.00000000	143.00000000
HRTRATE	HEART RATE BEATS/MIN.	75	77.12000000	19.74086172	55.00000000	203.00000000
---------- PATIENT NUMBER=116 TREATMENT CODE=15 MG WEEK NUMBER=4 ----------						
SYS	SYSTOLIC PRESSURE MMHG	118	129.83559322	19.46404323	87.00000000	170.00000000
DIAS	DIASTOLIC PRESSURE MMHG	118	98.53389831	19.98789471	63.00000000	141.00000000
HRTRATE	HEART RATE BEATS/MIN.	118	77.50847458	8.16679305	64.00000000	95.00000000
---------- PATIENT NUMBER=162 TREATMENT CODE=15 MG WEEK NUMBER=-2 ----------						
SYS	SYSTOLIC PRESSURE MMHG	88	153.43181818	16.08440056	110.00000000	201.00000000
DIAS	DIASTOLIC PRESSURE MMHG	88	109.65909091	15.62409454	82.00000000	144.00000000
HRTRATE	HEART RATE BEATS/MIN.	88	84.89772727	8.62639597	68.00000000	104.00000000
---------- PATIENT NUMBER=162 TREATMENT CODE=15 MG WEEK NUMBER=5 ----------						
SYS	SYSTOLIC PRESSURE MMHG	145	123.84137931	17.89889658	73.00000000	177.00000000
DIAS	DIASTOLIC PRESSURE MMHG	145	95.02758621	19.27611678	41.00000000	141.00000000
HRTRATE	HEART RATE BEATS/MIN.	145	83.87586207	12.86568662	60.00000000	115.00000000
---------- PATIENT NUMBER=163 TREATMENT CODE=20 MG WEEK NUMBER=-2 ----------						
SYS	SYSTOLIC PRESSURE MMHG	158	126.53164557	18.34512410	98.00000000	237.00000000
DIAS	DIASTOLIC PRESSURE MMHG	158	97.72151899	11.85306723	70.00000000	139.00000000
HRTRATE	HEART RATE BEATS/MIN.	158	82.96835443	18.51988805	58.00000000	188.00000000
---------- PATIENT NUMBER=163 TREATMENT CODE=20 MG WEEK NUMBER=4 ----------						
SYS	SYSTOLIC PRESSURE MMHG	184	118.85869565	12.33510387	88.00000000	185.00000000
DIAS	DIASTOLIC PRESSURE MMHG	184	66.45652174	12.24828344	39.00000000	143.00000000
HRTRATE	HEART RATE BEATS/MIN.	184	90.02173913	23.08108698	51.00000000	208.00000000

*REPRESENTS THE NUMBER OF READINGS TAKEN OVER EACH RECORDING PERIOD.

[illegible]

0165

TABLE 44 (CONT.)

TABLE 45
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence†	Worst Occurrence††
PN 5 mg	115	Headache	-1 - Mild		
		Drowsy	1 - Mild		
		Fatigue	1 - Mild		
		Dizziness	4 - Mild	5 - Mild	
	153	Dizziness	1 - Mild		
	165	Headache	-3 - Moderate	-1 - Moderate	
	306	Headache	1 - Moderate		
		Constipation	1 - Moderate		
	312	Nocturia	4 - Mild	5 - Mild	
	319	Joint Pain	-3 - Mild	-1 - Mild	
		Lower Back Pain	1 - Mild	3 - Mild	
		Ear Blockage	5 - Mild		
	323	Rash	-3 - Moderate	-1 - Moderate	
		Angina	-2 - Mild	-1 - Mild	
		Heart Flutter	1 - Moderate		
		Nausea	1 - Moderate		
	326	Impotence	-3 - Severe	5 - Severe	
	354	Pollakiuria	-3 - Moderate	-2 - Moderate	
		Polyuria	-3 - Moderate	-2 - Moderate	
		Joint Pain	3 - Mild	4 - Mild	
	357	Cough	-3 - Mild	-2 - Mild	
		Impotence	-3 - Mild	5 - Mild	
		Dyspnea	-3 - Mild	5 - Mild	
		Fatigue	1 - Mild		
	414	Pain Upper Left Arm	-3 - Moderate		
	419	Sleepy	2 - Moderate	3 - Moderate	
	424	URI	3 - Mild		
	454	Fatigue	3 - Mild		
	463	Right Chest Pain	1 - Moderate		
	504	Cold Symptoms	-3 - Mild		
		Headache	-1 - Mild	3 - Mild	
		Sneezing	2 - Mild		
		Indigestion	4 - Mild		
	506	Headache	1 - Mild	3 - Mild	
	554	Nasal Congestion	-3 - Mild		
		Cold Symptoms	1 - Mild	5 - Mild	
		Dizziness	1 - Mild		
		Swollen Ankles	1 - Mild		
		Sick to Stomach	1 - Mild	2 - Mild	
		Headache	3 - Moderate		
	559	Headache	-1 - Mild		
		Lightheadedness	2 - Mild	3 - Mild	
	606	Irritability	-2 - Moderate	2 - Mild	
		Nasal Congestion	-2 - Moderate	5 - Mild	
		Sinusitis	1 - Mild		
		Facial Flushing	2 - Mild		
		Arthritis	2 - Moderate		
		Wheezing	5 - Moderate		

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.

TABLE 45 (Continued)
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence†	Worst Occurrence††
PN 5 mg (cont'd)	613†††	Aneurysm	4 - Severe		
		Bypass Graft	4 - Severe		
	618	Cold	-3 - Moderate		
		Head Full Feeling	-2 - Mild		
		Headache	-1 - Moderate	1 - Mild	
		Cool Extremities	-1 - Mild	3 - Mild	
		Dryness of Skin	-1 - Mild	3 - Mild	
		Rash	1 - Mild	3 - Mild	
		Joint Pain	2 - Mild	5 - Mild	
		Constipation	4 - Mild		
		Flushing	1 - Mild		
	654	Lower Back Pain	-2 - Moderate		
		Headache	-2 - Mild	4 - Mild	
	659	Headache	2 - Mild	3 - Moderate	
PN 10 mg	108	Urinary Tract Infec.	-1 - Mild	1 - Mild	
		Pretibial Edema	4 - Mild	5 - Mild	
	155	Peripheral Edema	1 - Mild	3 - Mild	
	158	Pretibial Edema	-2 - Mild	2 - Mild	
		Nausea	-2 - Mild	-1 - Mild	
		Headache	-2 - Mild	2 - Moderate	1 - Moderate
	218	Headache	2 - Moderate		
		Pedal Edema	2 - Moderate		
	302	Heartburn	-3 - Moderate	3 - Mild	
		Nausea	-3 - Moderate		
	307	Nervousness	-3 - Moderate		
		Headache	1 - Moderate	2 - Severe	
	316	Right Knee Pain	-3 - Mild	-1 - Mild	
		Nocturia	-2 - Mild	5 - Mild	4 - Moderate
		Polyuria	-1 - Mild	5 - Mild	4 - Moderate
		Right Knee Swelling	2 - Moderate		
	324	Sensory Loss	-3 - Mild	3 - Mild	-1 - Moderate
		Joint Pain	-3 - Mild	3 - Mild	-1 - Moderate
		Sweating Loss	-3 - Mild	5 - Mild	-1 - Moderate
		Headache	3 - Moderate	4 - Mild	
		Muscle Cramps	4 - Mild	5 - Mild	
	329	Sinusitis	-3 - Moderate	3 - Mild	
		Heartburn	-3 - Moderate	3 - Mild	
	355	Headache	-3 - Mild		
	359	Sore Throat	3 - Mild		
	411	Skin Rash	1 - Severe	3 - Severe	
		Constipation	1 - Mild		
		Headache	3 - Severe		
	459	Earache	1 - Moderate	2 - Moderate	
	555	Headache	2 - Mild		
	-	Pollakiuria	4 - Mild		
		Nocturia	4 - Mild		

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.
†††Patient had bypass surgery following Week 4

TABLE 45 (Continued)
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence†	Worst Occurrence††
PN 10 mg (cont'd)	558	Allergic Rhinitis	-2 - Moderate	1 - Moderate	
		Headache	1 - Severe		
	601	Headache	-3 - Mild	4 - Mild	-1 - Moderate
		Nausea	-3 - Mild		
	610	Edema	-2 - Mild		
	611	Headache	-1 - Moderate		
	617	Nasal Congestion	2 - Severe	4 - Moderate	
		Headache	2 - Moderate		
		Pain in Knees	3 - Moderate		
	622	Headache	-5 - Moderate	5 - Moderate	
		Sinusitis	-4 - Moderate	4 - Moderate	
		Indigestion	-3 - Moderate	5 - Moderate	
		Edema	5 - Mild		
		Nasal Congestion	5 - Moderate		
	655	Edema	-3 - Mild	4 - Mild	
		Pounding in Head	-3 - Mild		
		Headache	-1 - Moderate	1 - Mild	
		Palpitations	1 - Mild		
		Fatigue	2 - Mild		
		Rash - Upper Extremities	3 - Mild	4 - Mild	
		Contact Dermatitis	5 - Moderate		
	658	Toothache	1 - Severe	2 - Mild	
		Atherosclerosis	1 - Mild	4 - Mild	
PN 15 mg	102	Fatigue	-3 - Mild	- - Mild	
		Peripheral Edema	5 - Mild		
	112	Gout	1 - Severe	5 - Mild	
		Broken Arm	3 - Severe		
		Indigestion	5 - Mild		
	116	Pretibial Edema	4 - Mild	5 - Mild	
	151	Headache	2 - Mild		
	202	Dizziness	1 - Mild	2 - Mild	
		Nervousness	2 - Moderate	3 - Moderate	
	309	Kidney Pain	-3 - Mild	4 - Mild	
		Pollakiuria	-3 - Mild	4 - Mild	
		Heartburn	-3 - Mild	4 - Mild	
		Chest Cyst	2 - Moderate	4 - Mild	
		Headache	3 - Mild	5 - Mild	4 - Moderate
	317	Right Ankle Edema	-3 - Mild	2 - Mild	
		Headache	4 - Mild	5 - Mild	
	322	Lower Back Pain	-3 - Moderate	5 - Mild	
		Shoulder Pain	-3 - Mild	5 - Mild	4 - Moderate
		Headache	1 - Mild	2 - Mild	
		Flushing	1 - Mild	5 - Mild	
		Lethargy	5 - Mild		

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.

TABLE 45 (Continued)
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence?	Worst Occurrence??
PN 15 mg (cont'd)	353	Headache	-3 - Mild	3 - Mild	-2 - Moderate
		Flushing	2 - Moderate	3 - Mild	
	356	Left Shoulder Pain	1 - Mild	4 - Mild	3 - Moderate
		Left Leg Pain	1 - Mild		
		Ankle Edema	3 - Moderate		
	361	Headache	2 - Mild	3 - Moderate	3 - Moderate
	403	Sore Throat	-3 - Moderate		
		Headache	-3 - Moderate		
		Chest Pain	1 - Moderate	3 - Mild	
		SOB on Exertion	1 - Moderate	3 - Mild	
		Lethargy	1 - Moderate	3 - Mild	
		Right Knee Swelling	1 - Moderate	3 - Moderate	
		Nasal Congestion	2 - Mild		
	409	Headache	3 - Moderate	3 - Mild	
	417	Headache	-3 - Mild	3 - Moderate	
		Broken Vessel Left Eye	-2 - Severe	1 - Severe	
	432	Diarrhea	-3 - Mild		
		Head Cold	-1 - Mild	1 - Mild	
		Flushing	1 - Mild	3 - Mild	
		Nasal Stuffiness	1 - Mild	3 - Mild	
		Dizziness	1 - Mild	3 - Mild	
	457	Hands Tingling	-3 - Severe		
		Swelling	-3 - Severe		
		Weight Gain	-3 - Severe		
		Dizziness	1 - Moderate	3 - Mild	
		Perspiration	1 - Severe		
	467	Swelled L. Hand	4 - Moderate	3 - Moderate	
	505	Headache	-3 - Mild	4 - Mild	
		Nasal Congestion	2 - Mild		
		Cold Symptoms	4 - Mild	3 - Mild	
	508	Headache	-1 - Mild	4 - Mild	
		Cold Symptoms	3 - Mild		
	512	Cold Symptoms	2 - Mild	3 - Mild	
	552	Muscle Spasm Chest	3 - Moderate		
	605	Headache	-1 - Moderate		

?Presented only if there are multiple occurrences.
??Presented only if different from information recorded under first or last occurrence.

TABLE 45 (Continued)
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence†	Worst Occurrence††
PN 15 mg (cont'd)	607	Headache	-4 - Mild	5 - Severe	
		Nausea	-2 - Mild	2 - Moderate	
		Chest Pain	-2 - Mild	5 - Moderate	
		Loose Stools	2 - Moderate		
		Dizziness	1 - Mild		
		Numbness Right Arm	1 - Mild		
	612	Headache	-1 - Mild		
	620	Arthritis	-3 - Moderate	2 - Moderate	
		Chest Pain	-2 - Moderate		
		Cold	2 - Moderate		
		Sinusitis	3 - Moderate		
		Headache	4 - Mild	5 - Mild	
	621	Back Pain	4 - Moderate		
	652	Nervousness	-3 - Moderate	5 - Moderate	
		Headache	-3 - Mild		
		Anxiety	3 - Moderate		
		Palpitations	4 - Moderate	5 - Moderate	
PN 20 mg	114	Rash	-1 - Mild	3 - Mild	
	210	Palpitations	3 - Moderate		
		Fatigue	3 - Moderate		
	225	Insomnia	1 - Moderate	5 - Mild	
	301	Dizziness	-3 - Mild	-2 - Mild	
		Headaches	5 - Moderate		
	308	Dizziness	-3 - Moderate	2 - Mild	
		Lower Back Pain	-2 - Moderate	-1 - Mild	
		Abrasions	-2 - Moderate	-1 - Mild	
		Palpitations	5 - Moderate		
	311	Pollakiuria	3 - Mild		
		Viral Infection	4 - Moderate		
		Toothache	4 - Severe	5 - Moderate	
		Facial Edema	4 - Severe	5 - Moderate	
		Nasal Stuffiness	5 - Mild		
		Constipation	5 - Mild		
		Decr. Appetite	5 - Mild		
		Cough	5 - Mild		
	320	Impotence	-3 - Moderate	5 - Mild	
		Insomnia	-3 - Mild	1 - Mild	-2 - Severe
		Arthritis	1 - Mild	5 - Mild	

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.

TABLE 45 (Continued)
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence†	Worst Occurrence††
PN 20 mg (cont'd)	321	Dizziness	-3 - Moderate	5 - Mild	
		Headaches	-3 - Moderate	5 - Mild	
		Blurred Vision	1 - Mild	3 - Mild	
		Tired Legs	4 - Moderate		
		Discomfort Left Hand	5 - Moderate		
	327	Nasal Congestion	-3 - Mild	-2 - Mild	
		Joint Pain	2 - Mild	5 - Mild	
	332	Chest/Back Pain	-3 - Moderate		
		Urinary Frequency	1 - Moderate		
	351	Flushing	1 - Moderate	5 - Mild	
		Ankle Edema	2 - Mild	5 - Moderate	
		Fatigue	2 - Mild	3 - Moderate	
	358	Sinusitis	-3 - Moderate		
		Polydypsia	-3 - Mild		
		Nocturia	-3 - Mild		
		Headache	1 - Mild	5 - Moderate	
	410	Palpitations	1 - Moderate	2 - Moderate	
		Redness on Extremities	2 - Mild	5 - Mild	
		Edema	2 - Mild	5 - Mild	
	422	Cramps	-3 - Moderate	-2 - Mild	
		Diarrhea	-3 - Moderate	-2 - Mild	
		Headache	-3 - Mild		
		Chest/Back Pain	3 - Mild	5 - Mild	
		Sinusitis	3 - Mild		
	456	Stomach Virus	-2 - Mild		
	465	Anxiet-	-2 - Severe	5 - Moderate	
		Headach	-2 - Moderate	2 - Severe	
		Fatigue	2 - Moderate	3 - Moderate	
		"Orange Color" on Lower Leg	3 - Mild	5 - Mild	4 - Moderate
		Cramps	4 - Moderate	5 - Moderate	
		Swelled Feet and Leg	4 - Mild		
	469	Decreased Libido	2 - Mild	5 - Mild	
	501	Swelling Feet	2 - Mild		
		Sore Throat	4 - Mild		
		Postnasal Drip	4 - Mild		
		Cough	4 - Mild		
	511	Cold Symptoms	3 - Mild	4 - Mild	
		Eye Object Removal	4 - Mild	5 - Mild	
	551	Headache	1 - Mild	2 - Moderate	
		Generalized Ache	2 - Mild		
	557	Cold Symptoms	-2 - Mild		
		Headache	2 - Mild		
		Tiredness	2 - Mild		
		Loss of Equilibrium	4 - Mild		
	604	Headache	-3 - Mild	2 - Mild	
		Sinusitis	1 - Mild	2 - Mild	
		Heartburn	3 - Moderate		
	609	Tightness in Chest	1 - Mild		
		Diarrhea	1 - Mild		
		Nervousness	1 - Mild		
		Fatigue	5 - Mild		

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.

TABLE 49 (Continued)
PN 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of First Occurrence	Last Occurrence†	Worst Occurrence††
PN 20 mg (cont'd)	615	Cold	-3 - Moderate		
		Increased Pulse	1 - Mild		
		Nervousness	1 - Moderate		
		Chest Pain	2 - Severe		
	616	Intestinal Virus	-3 - Mild		
		Headache	1 - Severe		
		Rapid Pulse	2 - Mild		
		Edema	2 - Mild	5 - Mild	
		Palpitations	3 - Mild		
	651	Chest Pain	1 - Moderate		
		Shortness of Breath	1 - Moderate		
		Tiredness	3 - Moderate		
	657	Cold	-3 - Mild		
		Headache	-2 - Mild	2 - Moderate	
		Palpitations	2 - Mild	4 - Mild	
		Muscle Aches	3 - Mild		
		Nocturia	3 - Mild		
		Flushing	4 - Mild		
		Anxiety	4 - Mild		
Placebo	104	Dizziness	4 - Mild		
	113	Swollen Hands, Ankles	-2 - Mild		
		Headache	1 - Moderate	2 - Moderate	
	117	Lightheadedness	-2 - Moderate		
		Headache	-2 - Moderate	-1 - Moderate	
		Nervousness	-2 - Moderate		
		Edema - Feet	3 - Moderate		
	155	Diarrhea	-1 - Moderate		
		Tachycardia	1 - Severe	2 - Severe	
		Dyspnea	1 - Severe	2 - Severe	
		Diaphoresis	1 - Severe	2 - Severe	
		Fatigue	2 - Mild	3 - Mild	
	161	Chest Pain	3 - Mild		
	304	Muscle Discomfort	2 - Moderate	4 - Mild	
	310	Numbness - Left Arm	-3 - Mild	-2 - Mild	
	314	Chronic Obstructive Pulm. Disease	-3 - Moderate	-2 - Moderate	
		Cyst	-3 - Moderate	-2 - Mild	
		Shortness of Breath	2 - Mild		
		Dyspnea	3 - Mild	3 - Mild	
		Cough	2 - Mild	3 - Mild	
	318	Heartburn	-3 - Moderate	-1 - Moderate	
		Nasal Congestion	-3 - Moderate	-1 - Moderate	
		Headache	2 - Mild	3 - Mild	
	331	Rash	-2 - Mild	-1 - Mild	

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.

TABLE 45 (Continued)
[illegible] 200-110 STUDY NO. 301

ADVERSE REACTION LISTING

Treatment Group	Patient Number	Adverse Reaction	Week and Severity of		
			First Occurrence	Last Occurrence†	Worst Occurrence††
Placebo (cont'd)	352	Cysts - Scalp	-1 - Moderate		
	404	Skin Peeling on Wrists	3 - Mild	5 - Mild	
	407	Urinary Frequency	-3 - Severe	-2 - Severe	
		Fatigue	-3 - Mild	2 - Mild	
	412	Headache	-3 - Moderate		
	453	Headache	2 - Mild	4 - Mild	
		Coughing	4 - Mild	5 - Mild	
	458	Dizziness Post Dose	-3 - Mild	2 - Mild	
	461	Headache	-2 - Moderate		
	503	Viral Infection	3 - Moderate		
		Upset Stomach	3 - Mild		
		Headache	3 - Mild		
		Cold	3 - Mild		
	510	Rt. Otitis Media	-2 - Moderate	1 - Mild	
		Rt. Earache	-3 - Moderate	-1 - Mild	
		Headache	-3 - Moderate	-2 - Moderate	
		Edema - Extremities	3 - Mild	4 - Mild	
	515	Toothache	5 - Mild		
		Cold Symptoms	-2 - Mild		
	553	Cold Symptoms	3 - Moderate	5 - Mild	
	556	Cold Symptoms	-3 - Mild	4 - Mild	
		Epigastric Pain	-3 - Mild	1 - Mild	
	600	Dizziness	-3 - Mild	3 - Mild	
		Tiredness	-1 - Mild	2 - Mild	
		Constipation	3 - Mild		
		Right Shoulder Pain	3 - Moderate		
		Blurred Vision	3 - Mild		
		Loss of Coordination	3 - Mild		
		Cough	4 - Mild		
	614	Headache	-4 - Mild		
		Sinusitis	-3 - Mild	4 - Mild	
		Nasal Congestion	1 - Mild		
		Leg Pain	2 - Mild		
		Neck Pain	4 - Mild		
	619	Headache	-2 - Severe	3 - Moderate	
		Exhaustion	1 - Mild	2 - Mild	
		Cough	1 - Mild	2 - Mild	
		Eczema	1 - Mild	3 - Mild	2 - Moderate
		Tendonitis - Left Bicep	1 - Mild	2 - Mild	
		Sunburn	3 - Moderate		
		Diarrhea	5 Moderate		
		Vomiting	5 - Moderate		
	656	Headache	-3 - Moderate	5 - Mild	
		Nausea	-2 - Moderate		
		Vomiting	-2 - Moderate		

†Presented only if there are multiple occurrences.
††Presented only if different from information recorded under first or last occurrence.

TABLE 46
PN 200-110 STUDY NO. 301

COMPARATIVE ADVERSE REACTION FREQUENCIES
ADJUSTED FOR BASELINE EFFECTS
(Weeks 1-5)

Adverse Reaction	PN 200-110 Treatment Group				Placebo Group (N=41)
	5 mg (N=40)	10 mg (N=40)	15 mg (N=41)	20 mg (N=41)	
Miscellaneous					
Arms, Misc. Abnorm.	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Ears Disorder	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Teeth/Mouth Pain	0 (0.0)	1 (2.5)	0 (0.0)	1 (2.4)	1 (2.4)
Throat Discomfort	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Skin					
Dermatitis	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	1 (2.5)	2 (5.0)	0 (0.0)	2 (4.9)	0 (0.0)
Skin (Misc. Abnorm.)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.4)
Musculo-skeletal					
Back, Ache/Pain	1 (2.5)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Chest/Back Pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Muscle Pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)
Tendinitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
Hand/Feet, Pain, Ache	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Joint Pain	2 (5.0)	1 (2.5)	0 (0.0)	1 (2.4)	0 (0.0)
Legs, Misc. Ache/Pain	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)	1 (2.4)
Muscle Spasm	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Neck Pain/Sore/Stiff	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
Pain, General	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Shoulder Pain	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)	1 (2.4)
Respiratory					
Coughing	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	4 (9.8)+
Nasal Congestion	0 (0.0)	2 (5.0)	3 (7.3)	1 (2.4)	1 (2.4)
Post Nasal Drip	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Sinusitis	1 (2.5)	0 (0.0)	1 (2.4)	2 (4.9)	0 (0.0)
Sneezing	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Throat, Pain/Numb	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Wheezing	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiovascular					
Breath, Short	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Cardiac (Misc. Abnorm.)	2 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest Pain	1 (2.5)	0 (0.0)	2 (4.9)	3 (7.3)	1 (2.4)
Cramps	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Dyspnea	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)+
Edema	1 (2.5)	6 (15.0)	5 (12.2)	6 (14.6)	3 (7.3)
Cramps, Legs/Feet	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Palpitation	0 (0.0)	1 (2.5)	1 (2.4)	5 (12.2)	0 (0.0)
Tachycardia	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	1 (2.4)

+p<0.05 for placebo vs. all PN 200-110 treatment groups combined.

TABLE 46 (Continued)
PN 200-110 STUDY NO. 301

COMPARATIVE ADVERSE REACTION FREQUENCIES
ADJUSTED FOR BASELINE EFFECTS
(Weeks 1-5)

Adverse Reaction	PN 200-110 Treatment Group				Placebo Group (N=41)
	5 mg (N=40)	10 mg (N=40)	15 mg (N=41)	20 mg (N=41)	
Gastrointestinal					
Abdominal Discomfort	1 (2.5)	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Constipation	2 (5.0)	1 (2.5)	0 (0.0)	1 (2.4)	1 (2.4)
Diarrhea	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)
Nausea	2 (5.0)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.4)
Stools, Loose	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Vomiting	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
Urogenital					
Nocturia	1 (2.5)	2 (5.0)	0 (0.0)	1 (2.4)	0 (0.0)
Pollakiuria	0 (0.0)	2 (5.0)	0 (0.0)	2 (4.9)	0 (0.0)
Central Nervous System					
Anxiety	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Anorexia	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Coordination, Loss	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
Dizziness	4 (10.0)	0 (0.0)	4 (9.8)	0 (0.0)	1 (2.4)
Drowsy	2 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ears, Stopped/Popping	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Equilibrium, Loss	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Fatigue	3 (7.5)	1 (2.5)	0 (0.0)	6 (14.6)	2 (4.9)
Headache	4 (10.0)	8 (20.0)	9 (22.0)	6 (14.6)	4 (9.8)
Insomnia	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Lethargy	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)	0 (0.0)
Libido Decrease/ Frigidity	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Nervousness	0 (0.0)	0 (0.0)	1 (2.4)	2 (4.9)	0 (0.0)
Autonomic Nervous System					
Burning Sensation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
Flushing	2 (5.0)	0 (0.0)	3 (7.3)	2 (4.9)	0 (0.0)
Hyperhydrosis	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.4)
Visual Disturbance	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)
Total No. of Patients with an Adverse Reaction	19 (47.5)	17 (42.5)	23 (56.1)	23 (56.1)	16 (39.0)

TABLE 47
PN 200-110 STUDY NO. 01

COMPARATIVE ADVERSE REACTION FREQUENCIES
ADJUSTED FOR BASELINE DIFFERENCES
(Weeks 3-5)

Adverse Reaction	PN 200-110 Treatment Group				Placebo Group (N=39)
	5 mg (N=38)	10 mg (N=35)	15 mg (N=41)	20 mg (N=41)	
Miscellaneous					
Teeth/Mouth Pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.6)
Throat Discomfort	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Skin					
Dermatitis	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	1 (2.6)	2 (5.7)	0 (0.0)	2 (4.9)	0 (0.0)
Skin (Misc. Abnorm.)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.6)
Musculo-skeletal					
Back, Ache/Pain	1 (2.6)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Chest/Back Pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Muscle Pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.6)
Hand/Feet, Pain, Ache	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Joint Pain	2 (5.3)	1 (2.9)	0 (0.0)	1 (2.4)	0 (0.0)
Legs, Misc. Ache/Pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Muscle Spasm	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Neck Pain/Sore/Stiff	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Shoulder Pain	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)	1 (2.6)
Respiratory					
Coughing	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	3 (7.7)
Nasal Congestion	0 (0.0)	2 (5.7)	1 (2.4)	1 (2.4)	0 (0.0)
Post Nasal Drip	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Sinusitis	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Throat, Pain/Numb	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Wheezing	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiovascular					
Breath, Short	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Cardiac (Misc. Abnorm.)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest Pain	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)	1 (2.6)
Cramps	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Dyspnea	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Edema	0 (0.0)	3 (8.6)	5 (12.2)	5 (12.2)	3 (7.7)
Cramps, Legs/Feet	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
Palpitation	0 (0.0)	0 (0.0)	1 (2.4)	4 (9.8)	0 (0.0)

TABLE 47 (Continued)
PN 200-110 STUDY NO. 301

COMPARATIVE ADVERSE REACTION FREQUENCIES
ADJUSTED FOR BASELINE EFFECTS
(Weeks 3-5)

Adverse Reaction	PN 200-110 Treatment Group				Placebo Group (N=39)
	5 mg (N=38)	10 mg (N=35)	15 mg (N=41)	20 mg (N=41)	
Gastrointestinal					
Abdominal Discomfort	1 (2.6)	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Constipation	1 (2.6)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.6)
Diarrhea	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Nausea	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Vomiting	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Urogenital					
Nocturia	1 (2.6)	2 (5.7)	0 (0.0)	1 (2.4)	0 (0.0)
Pollakiuria	0 (0.0)	2 (5.7)	0 (0.0)	1 (2.4)	0 (0.0)
Central Nervous System					
Anxiety	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Anorexia	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Incoordination, Loss	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Dizziness	2 (5.3)	0 (0.0)	2 (4.9)	0 (0.0)	1 (2.6)
Drowsy	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Jars, Stopped/Popping	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Equilibrium, Loss	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Fatigue	1 (2.6)	0 (0.0)	0 (0.0)	5 (12.2)	1 (2.6)
Headache	3 (7.9)	2 (5.7)	7 (17.1)	2 (4.9)	3 (7.7)
Insomnia	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Lethargy	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)	0 (0.0)
Libido Decrease/ Frigidity	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)
Nervousness	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)
Autonomic Nervous System					
Burning Sensation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Flushing	0 (0.0)	0 (0.0)	3 (7.3)	2 (4.9)	0 (0.0)
Visual Disturbance	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1 (2.6)
Total No. of Patients with an Adverse Reaction	14 (36.8)	10 (28.6)	21 (51.2)	20 (48.8)	15 (38.5)

Figure 1

PN 200-110 STUDY #301
Supine Systolic BP
Change from Baseline

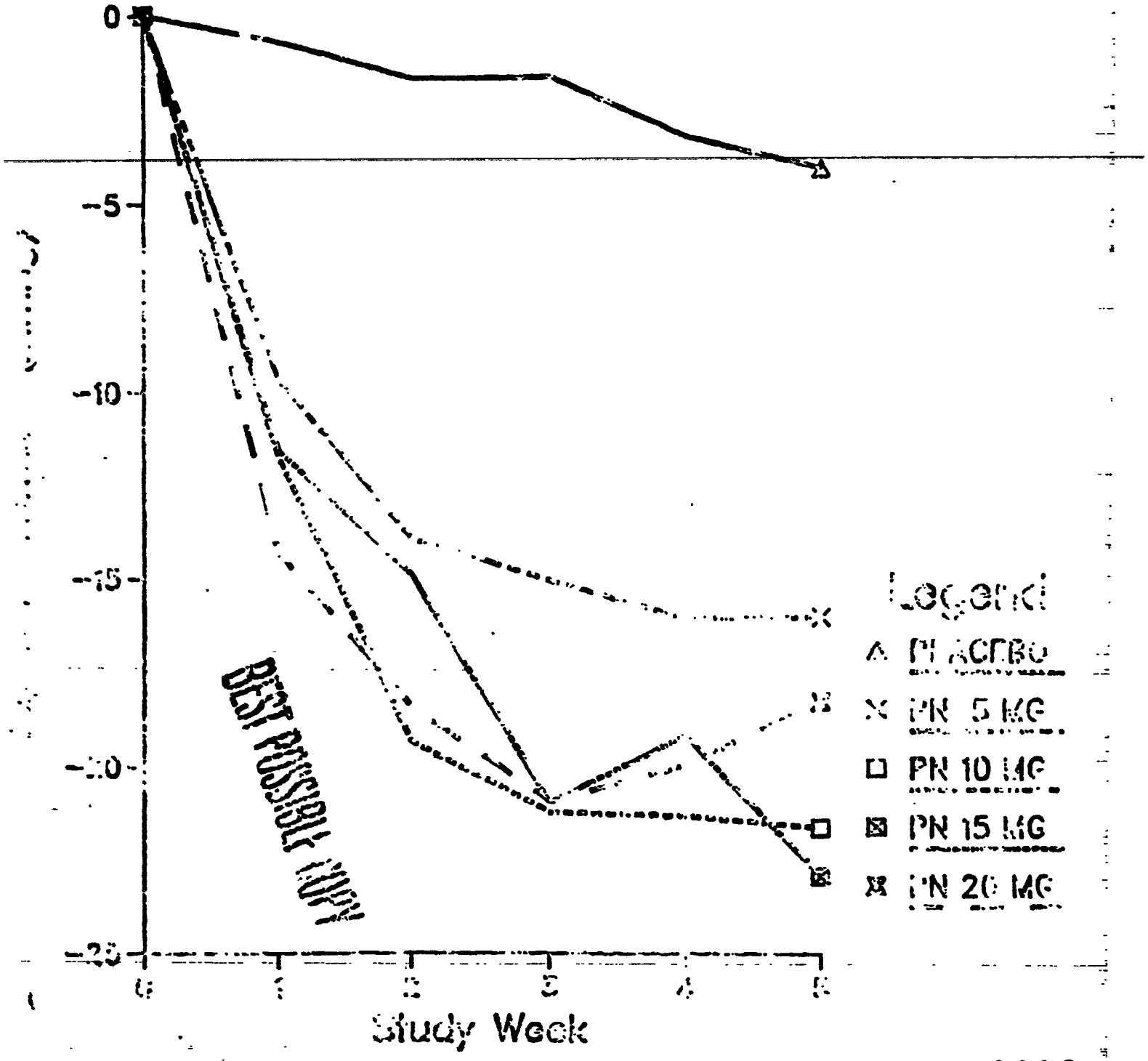

Figure 2

PN 200-110 STUDY #301
Supine Diastolic BP
Change from Baseline

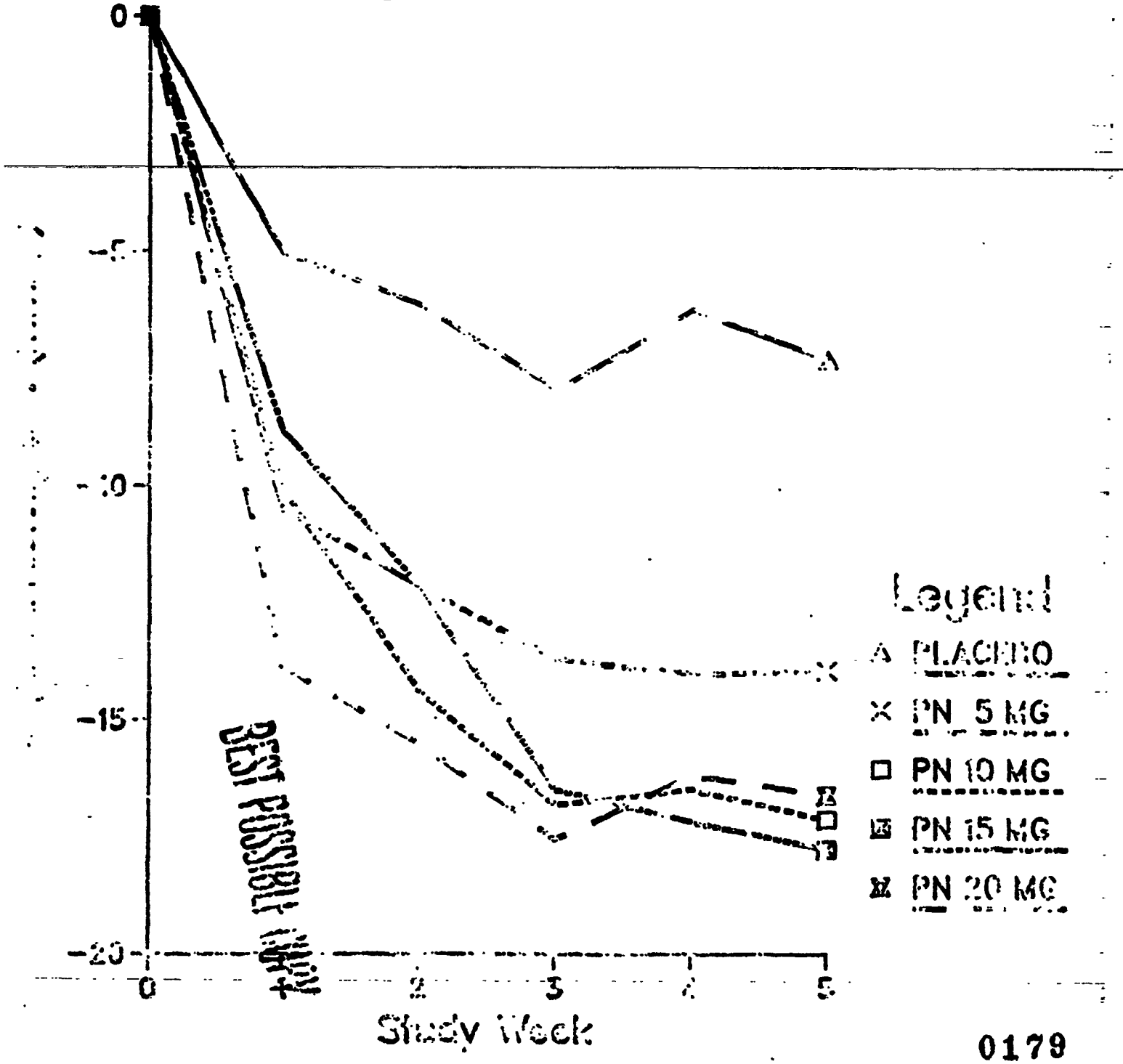

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Figure 3

PN 200-110 STUDY #301
Supine Pulse
Change from Baseline

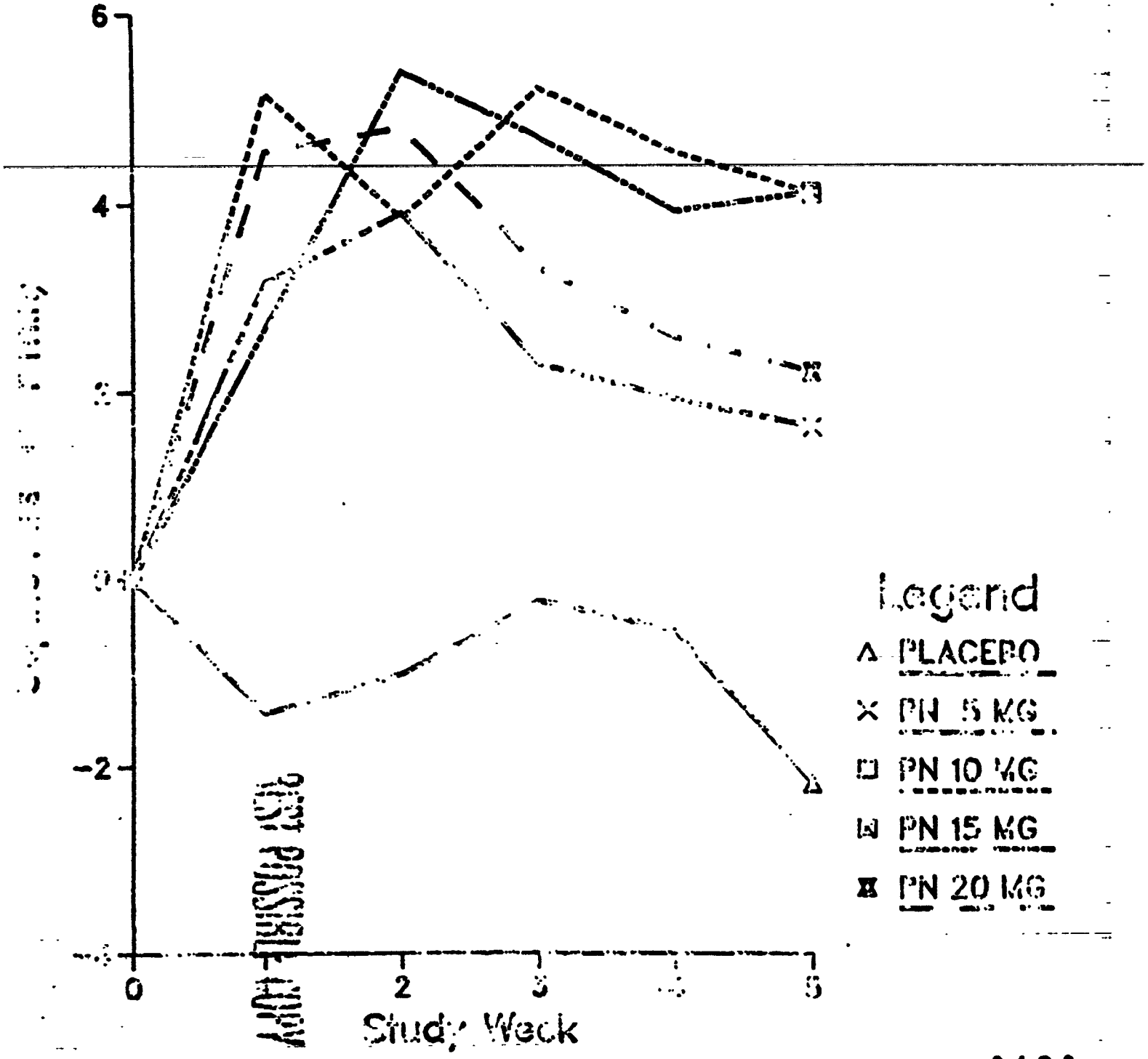

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Figure 4

PN 200-110 STUDY #301
Standing Systolic BP
Change from Baseline

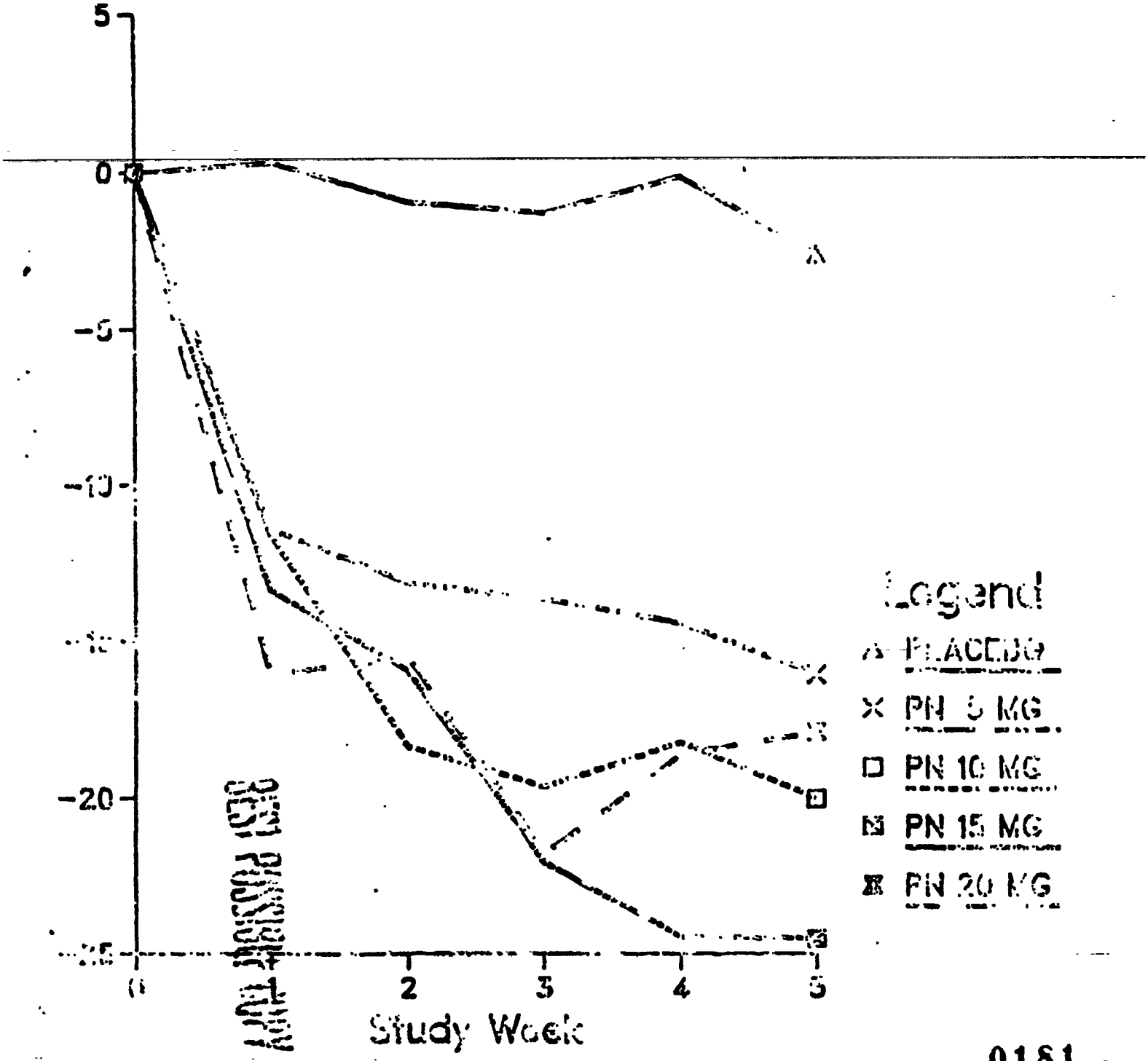

Figure 5

PN 200-110 STUDY #301
Standing Diastolic BP
Change from Baseline

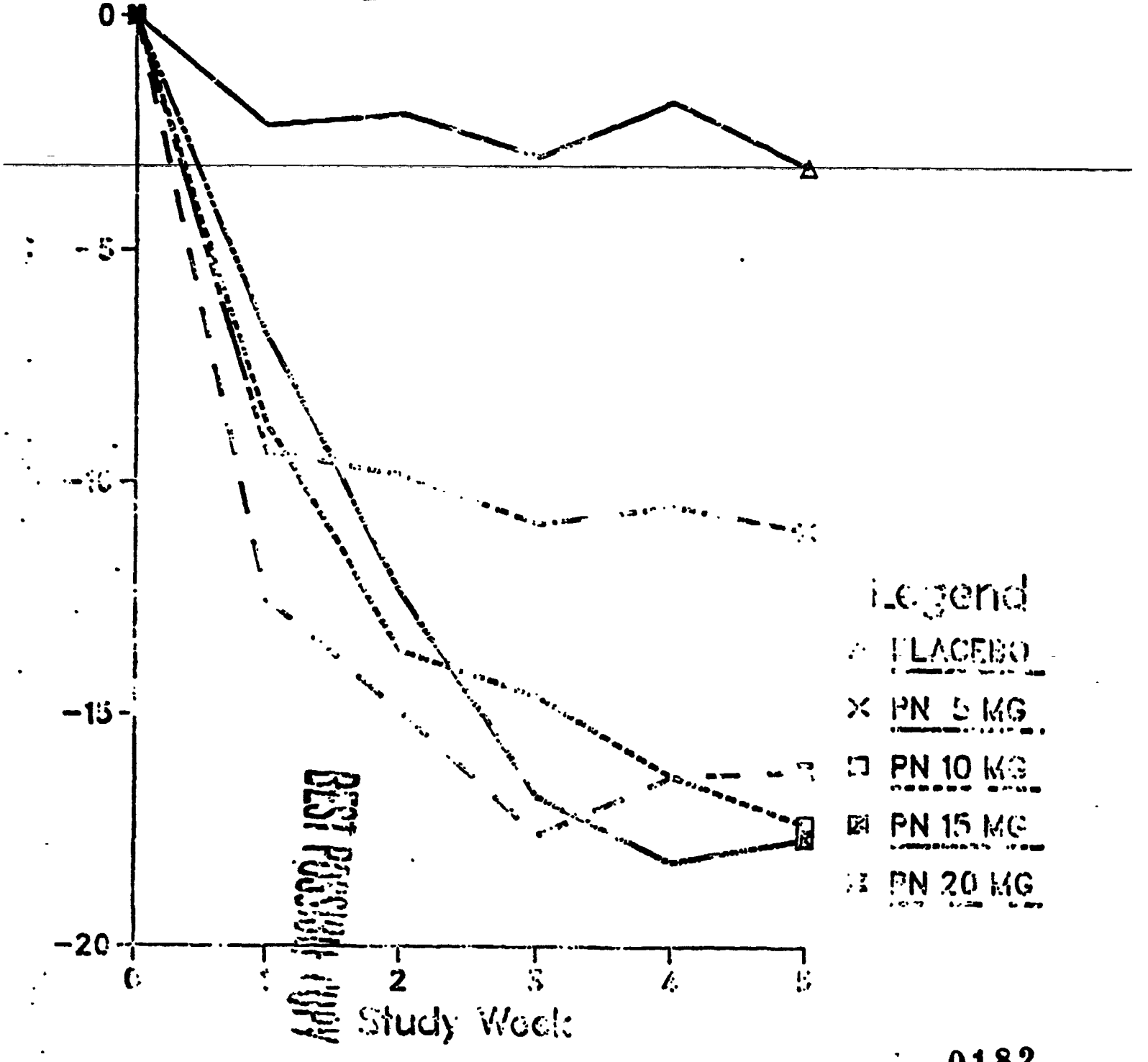

Figure 6

PN 200-110 STUDY #301
Standing Pulse
Change from Baseline

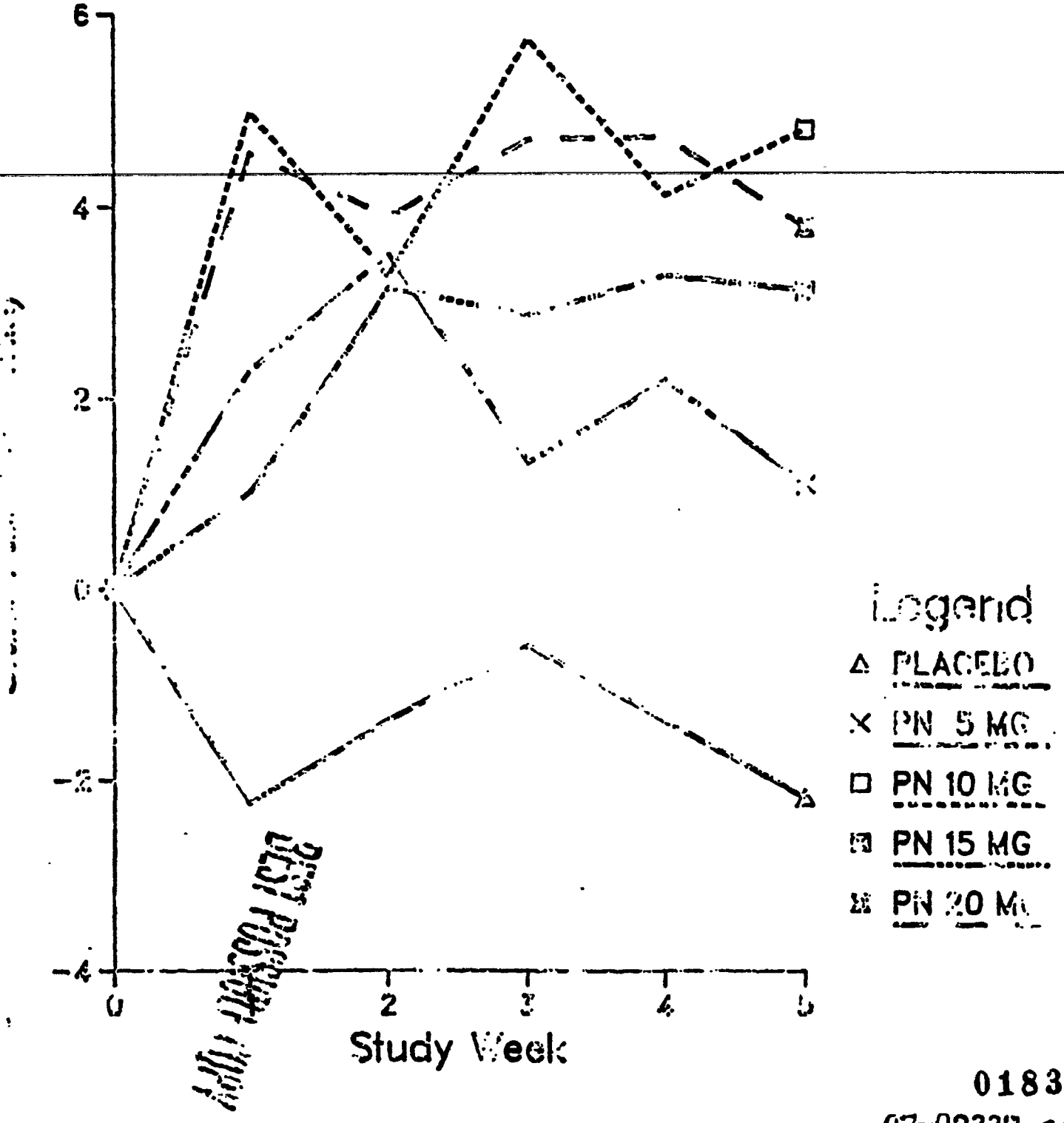

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Figure 7

PN 200-110 Study #301
Summary of 24 hour ambulatory monitoring
Patient 115
Treatment group is PN 5 MG

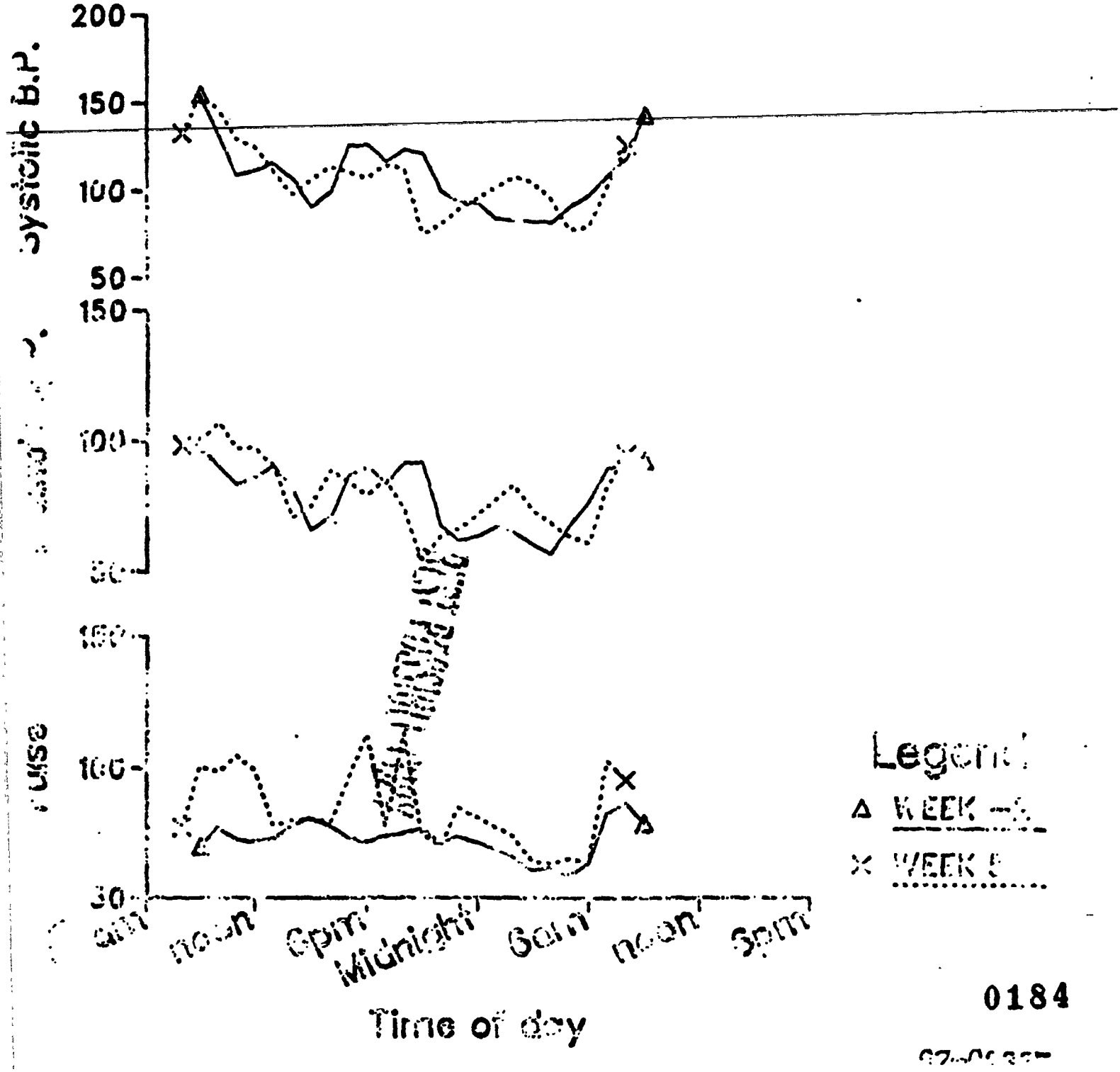

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Figure 8
PN 200–110 Study #301
ummary of 24 hour ambulatory monitoring
Patient 111
Treatment group is PN 10 MG

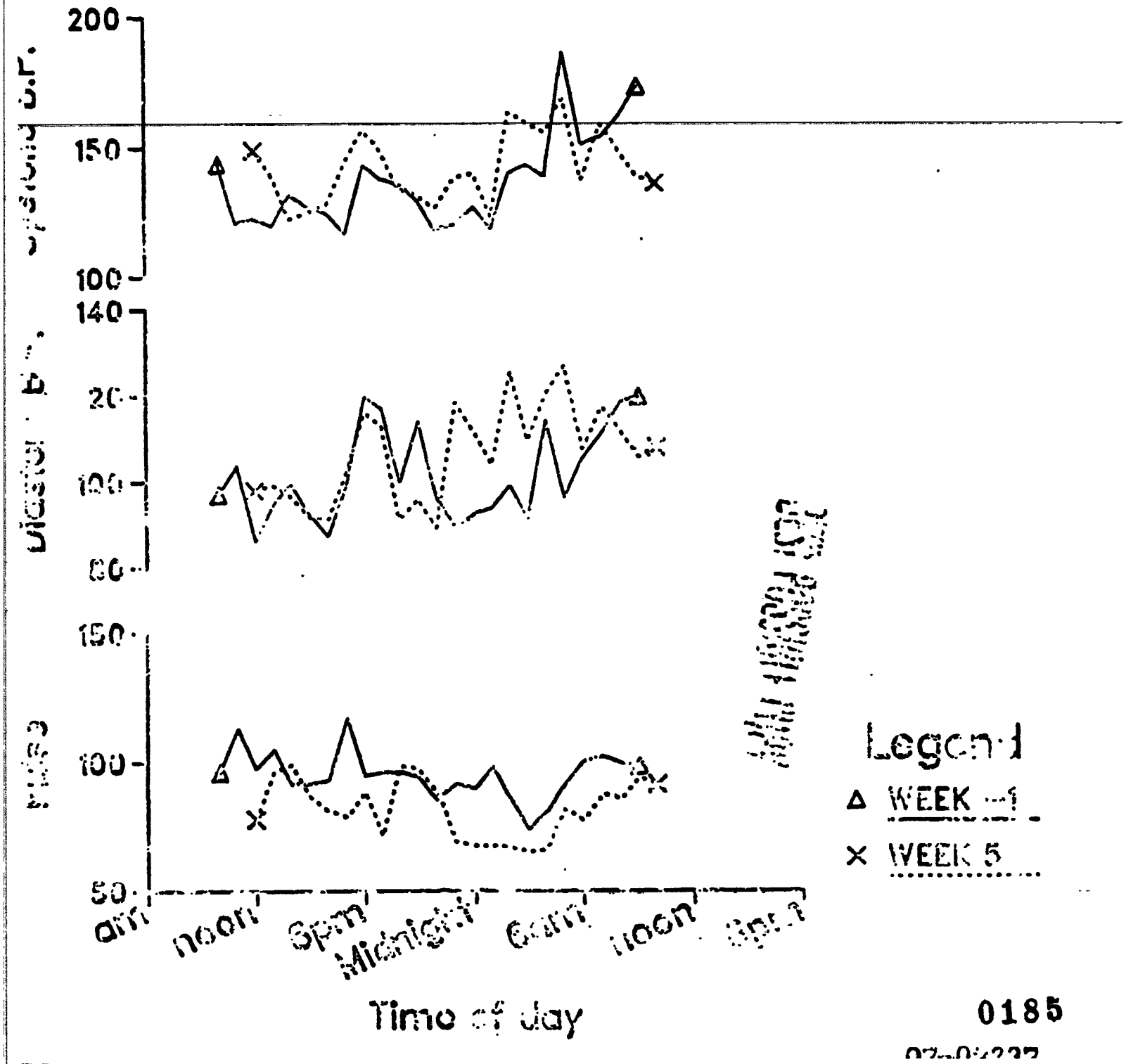

Figure 9

PN 200-110 Study #301

Summary of 24 hour ambulatory monitoring

Patient 116

Treatment group is PN 15 MG

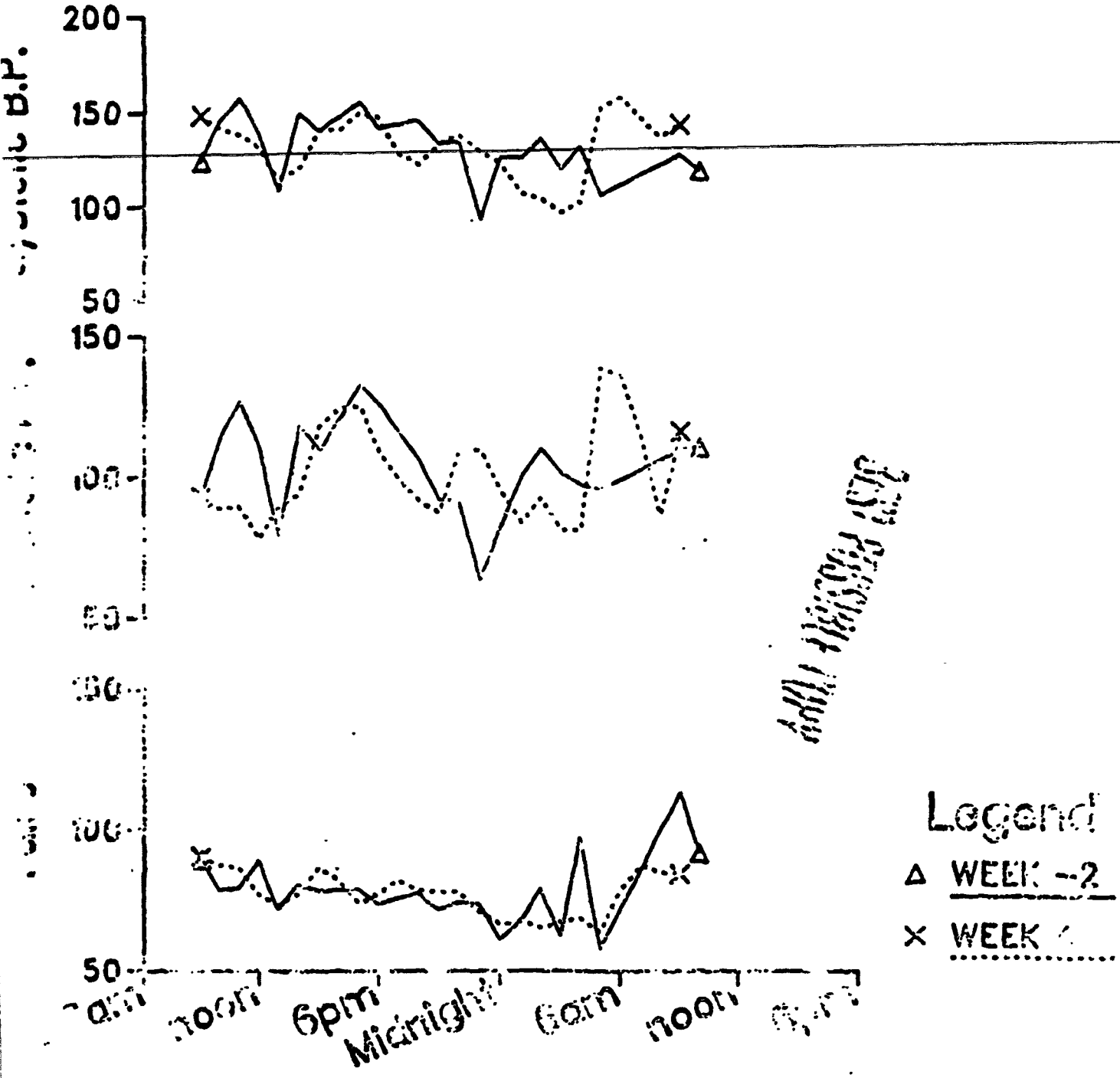

Figure 10

PN 200-110 Study #301
ummary of 24 hour ambulatory monitoring
Patient 162
Treatment group is PN 15 MG

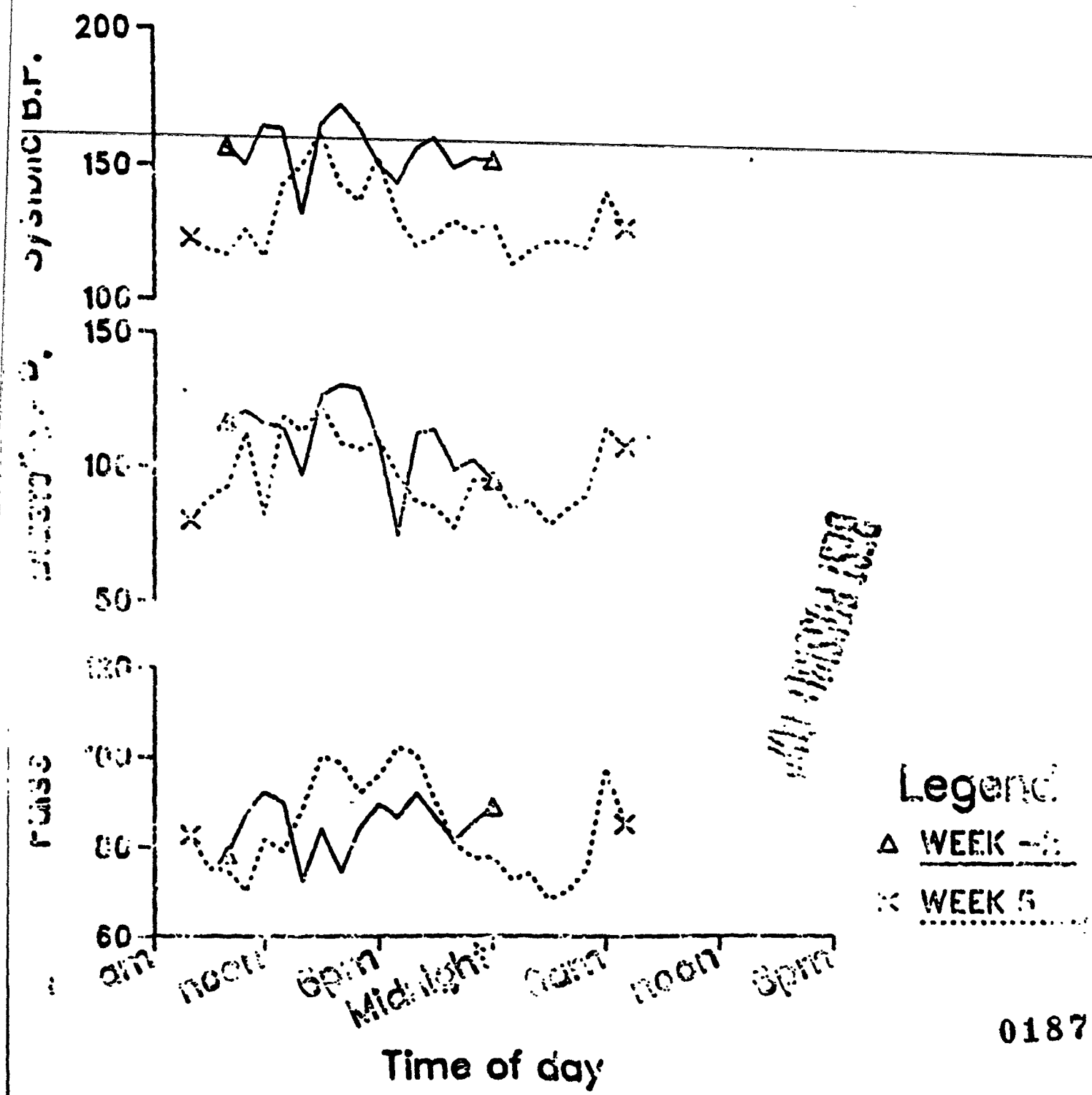

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Figure 11
PN 200-110 Study #301
Summary of 24 hour ambulatory monitoring
Patient 114
Treatment group is PN 20 MG

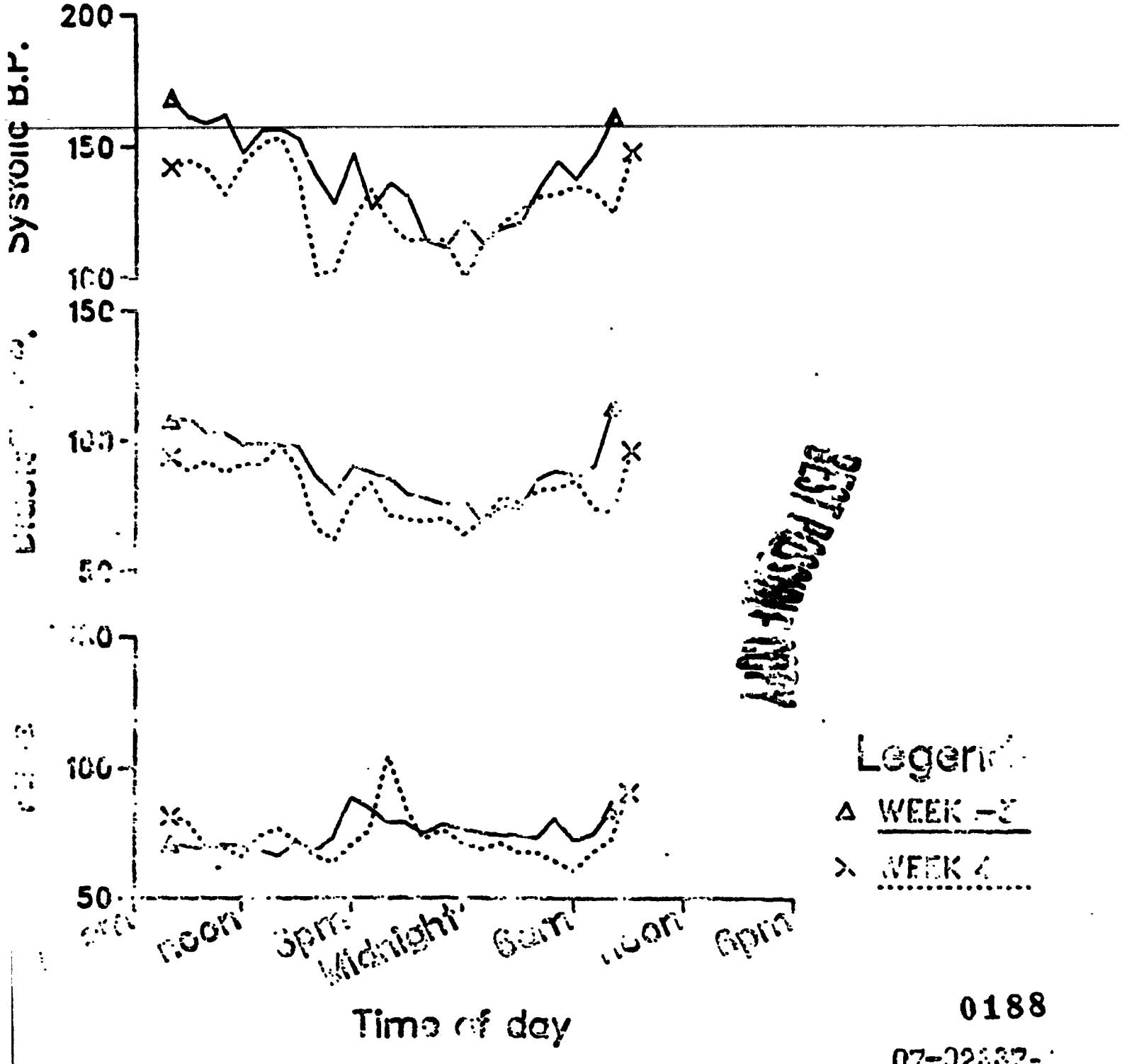


Figure 12
PN 200–110 Study #301
Summary of 24 hour ambulatory monitoring
Patient 163
Treatment group is PN 20 MG

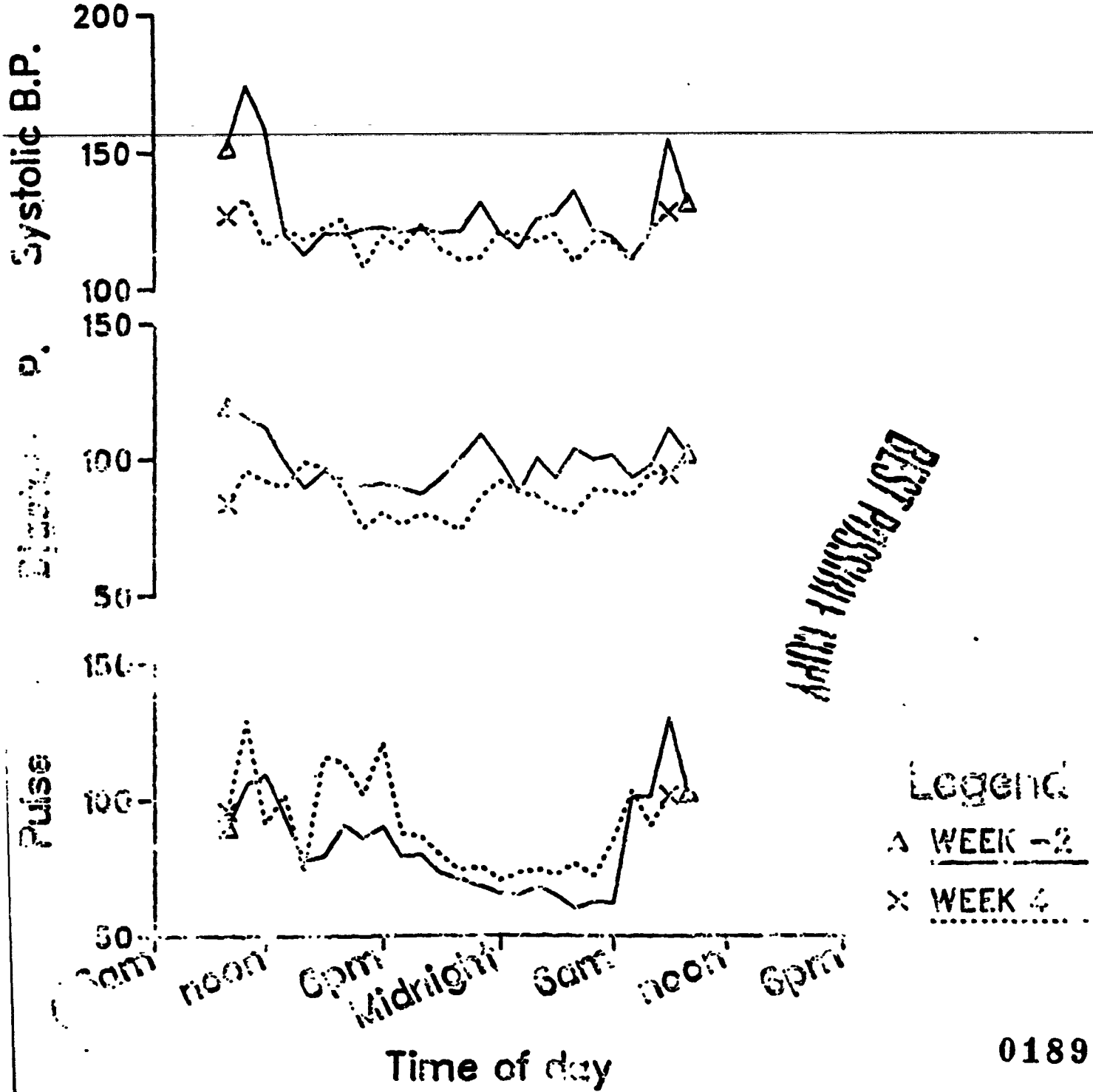
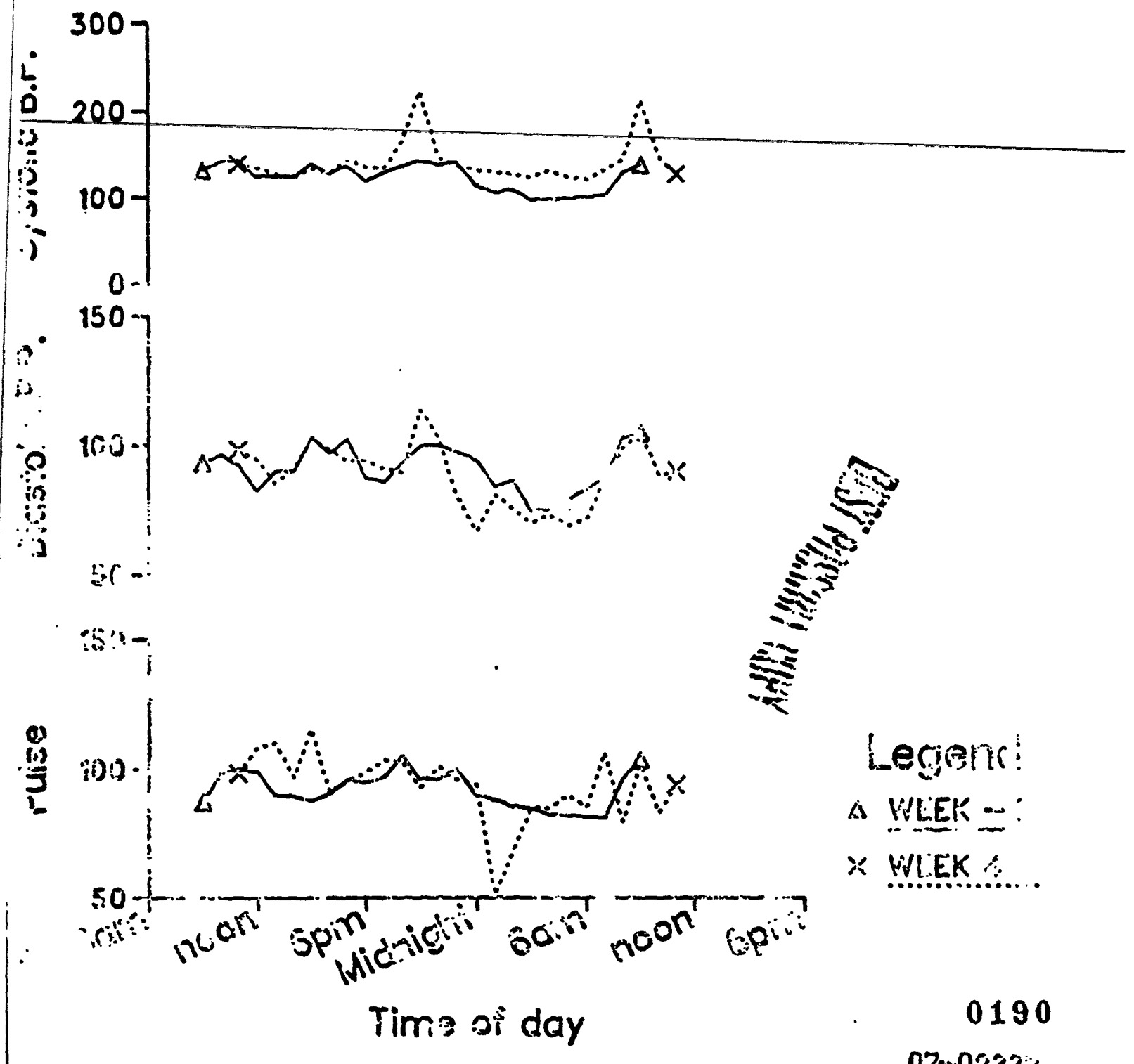


Figure 14
PN 200-110 Study #301
ummary of 24 hour ambulatory monitoring
Patient 113
Treatment group is Placebo



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07-02337

302

Protocol No.

Title

A Multicenter Evaluation of the Safety and Efficacy of PN [illegible] in the Treatment of Hypertension Compared to Propranolol

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Dates of Study: June 1, 1984 to June 14, 1986.

Objective

To evaluate the efficacy and safety of PN 200-110 (PN), 2.5 - 10.0 mg tid, in the treatment of hypertension compared to propranolol 60 - 240 mg bid.

Design

This was a multicenter, randomized, double blind, parallel group, propranolol controlled study.

Patient Population

Outpatients of either sex, over the age of 18 years, with benign essential hypertension were selected for this study. Each patient entered a preliminary 3 week placebo washout period, during which all previous antihypertensives were withdrawn and blood pressure was evaluated each week. In order to qualify for the double blind period, patients were to have an average sitting diastolic blood pressure (SDBP) of > 95 mm Hg on two consecutive visits during washout period. In addition, a decreasing trend in blood pressure was not to be observed. This was defined as an average SDBP at any evaluation of washout period being less than previous day and having decreased by > 10 mm Hg.

Exclusion criteria included secondary or malignant hypertension, SDBP > 120 mm Hg on two consecutive visits, angina pectoris, CHF, MI within 6 months of the study, arrhythmias, investigational drug within previous 4 weeks, any medication or disease that could interfere with evaluation of test drug, certain specified

medications, bradycardia, AV block > 1st degree, alcohol or drug abuse in previous 2 years, diabetes mellitus requiring insulin therapy, bronchial asthma, COPD or respiratory allergy, pregnant or lactating females.

Medications

Identically appearing capsules of either 2.5 mg PN or 60 mg propranolol were supplied. Study design and dosing schedule is shown in Table 1. For first three weeks, all patients received placebo bid. Doses of all study drugs were administered bid and at least 30 minutes prior to blood pressure being measured. Patients who satisfied entry criteria were stratified as in previous studies and randomized to PN or propranolol.

Initial dose of drugs were 2.5 mg bid (PN) or propranolol 60 mg bid. This was given during weeks 1 and 2. If SDBP > 90 mm Hg at this time, dose was increased to 5 mg bid or 120 mg bid respectively for weeks 3 and 4. Similarly, doses were increased for weeks 5 and 6 to 7.5 mg bid or 180 mg bid and for weeks 7 and 8, dose was 10 mg bid or 240 mg bid respectively. If average SDBP was < 90 mm Hg at end of weeks 2, 4 or 6 dose remained unchanged for next 2 weeks and, if then necessary was increased as described. If at any time SDBP > 110 mm Hg, dose could be increased after one week instead of two. From week 7, dose remained constant unless a reduction was required due to adverse reaction. At end of 10 weeks, medication was tapered.

Evaluations

Evaluations were done weekly as per Table 2. Method of recording blood pressures and pulse rate described in report. At Center B, left ventricular function was determined using echocardiography at weeks - 1 and 10. At Center C, ambulatory blood pressure determinations were done over 24 hour periods at week - 1 and week 10

Results.

A total of 89 patients were randomized to double blind phase. Of these, 68 were completely valid for analysis, 16 partially valid and 5 invalid. The reasons for not being completely valid are given in Table 4. There were 46 patients randomized to PN and 43 to propranolol. Table 5 summarizes data by center, by number of patients per group. Center A contributed 31% patients, center B 34% and center C 35% of total. The number of valid patients by week is shown below.

Week	1	2	3	4	5	6	7	8	9	10
PN	42	42	42	40	40	40	40	40	37	37
Propr	42	42	41	38	37	36	32	31	31	31
Total	84	84	83	78	77	76	72	71	68	68

The mean age of the patients was 50.7 years (19 - 76); 29 (33%) were white, 58 (65%) were black, 1 oriental and 1 other. There were 44 males and 45 females. Mean duration of hypertension was 11 years. With exception of body weight (higher in PN group), there were no statistically significant differences between groups.

Table 7 presents mean dose, by week for all valid patients and Table 8 presents similar data for partially valid group. During fixed dose period, mean dose was 12 mg PN and 332 mg propranolol. Table 9 summarizes data from analysis of interactions as well as efficacy results on investigator x treatment basis for each efficacy variable for weeks 7 - 10. There was a marginally ($p=0.065$) treatment x investigator interaction for sitting systolic blood pressure. Center B had greater decrease in PN group and less increase in propranolol group than other two centers.

Efficacy

Efficacy data were examined both between and within groups as well as by categorizing as in previous studies.

Weeks 1 - 2.

Tables 10 and 11 summarize data for this period with patients on lowest dose medication. PN reduced SDBP from baseline by 8.8 mm Hg week 1 and by 8.9 mm Hg week 2; the respective reductions for propranolol were 6.7 and 7.8 mm Hg. Reductions by both drugs were statistically significant from baseline but not between groups. The differences in pulse rate were statistically significant between groups with PN causing an increase in rate and propranolol a decrease.

Weeks 1 - 6 (Titration)

Table 12 presents these data for valid and partially valid patients. The reductions for both groups are statistically significant from baseline for all variables as well as being statistically significant between groups. The PN group reduced SDBP by 15.7 mm Hg compared to 9.0 mm Hg with propranolol. The increment in decrease over week 2 is more significant with PN than with propranolol. Once again, differences in pulse rate were as expected.

Weeks 7 - 10 (Fixed Dose)

Table 13 summarizes these data by week and Table 14 by endpoint. The average reduction in SDBP over weeks 7 - 10 was 15.4 (PN) and 10.0 propranolol. Reductions for both groups were statistically significant from baseline and there was statistically significant between group differences. The reductions at endpoint was 16.1 mm Hg (PN) and 10.2 mm Hg propranolol, once again significant. Results for pulse rate was similar to previous weeks.

Categorical Responses, as defined below, for valid patients at week 10 were:

	n =	1	2	3	4
PN	37	16 (43%)	13 (35%)	6 (16%)	2 (5%)
Propr	31	6 (19%)	6 (19%)	10 (32%)	9 (29%)

Category 1: SDBP < 85 mm Hg; 2: > 10 mm Hg but still > 85 mm Hg; 3: > 5 but < 10 mm Hg; 4: < 5 mm Hg or increase.

Over 80% (31/37) PN group had at least 10 mm Hg reduction in SDBP and 41% (15/37) had a decrease < 85 mm Hg over weeks 7 - 10. For propranolol, the figures were 19% and 26% respectively. PN was significantly more effective than propranolol.

Number of valid patients titrated to each dose level at week 10 was:

Group	n =	1	2	3	4
PN	37	8 22%	13 35%	10 27%	6 16%
Propr	31	7 23%	4 13%	8 26%	12 39%

Level 1; 5 mg PN or 120 mg propr; 2: 10 mg or 240 mg; 3: 15 mg or 360 mg; 4: 20 mg or 480 mg.

Only 16% PN received highest dose compared to 39% propranolol

All Patients - Endpoint Analysis

Table 15 summarizes results from analysis including all patients regardless of validity. These results are similar to those seen in Tables 13 and 14.

Figures 1 - 3 display all results for valid patients graphically.

Safety

Table 16 lists specific newly occurring abnormalities in physical examination. There were 15 abnormalities for PN and 4 with propranolol. Tables 17 and 18 list newly occurring cardiovascular abnormalities. These occurred in 30 PN and 17 propr patients.. One PN was withdrawn due to increased angina and shortness of breath. One propranolol was withdrawn due to bronchospasm. The frequencies of palpitation and abnormality on heart examination were higher with PN and dyspnea higher with propranolol. Incidence of edema similar for both groups but was more consistent with PN and appeared transient with propr.

Table 19 presents x-ray data and Table 20 ECG changes. There were 27 PN with newly occurring abnormalities and 25 in propranolol group. Tables 21 and 22 present frequencies and specific summaries for ECGs.

Clinical Laboratory Data

Tables 25 - 30 present data for laboratory changes. (Tables 25 and 26 hematology; 27 and 28 urine, 29 and 30 chemistry). The only statistically significant changes occurred in chemistries. The main parameters affected were inorganic phosphorous, BUN, uric acid, glucose, alkaline phosphatase, potassium and creatinine. The difference between groups for alkaline phosphatase was significant. The results were not clinically significant. Alkaline phosphatase was the most frequently occurring change for PN.

Adverse Reactions

Table 4 listed patients who withdrew and their reasons. Tables 37 and 38 list ADRs by patient and body system. Overall from weeks 1 - 10, 83% PN and 65% propranolol reported at least one newly occurring abnormality.. At week 2, the difference between groups was statistically significant (PN 28% vs propranolol 9%). The difference over the 10 weeks was marginally significant $p < .10$. The most frequent reported PN ADRs were in the central nervous and cardiovascular systems. In propranolol it was central nervous and gastrointestinal systems. The most frequently reported events are shown below:

ADR	PN n=46		Propranolol n = 43.		
Edema	8	17%	3	7%	
Palpitations	5	11%	0		•
Abdominal Discomfort	3	7%	6	14%	
Diarrhea	4	9%	4	9%	
Dizziness	4	9%	2	5%	
Fatigue	2	4%	7	16%	•
Headache	13	28%	6	14%	
Flushing	5	11%	0		•

• Between group differences $p < 0.10$

Echocardiography

Table 39 summarizes data from center B for echocardiographic results for both drugs. Statistically significant changes were observed in left ventricular diastolic dimensions, end diastolic volume, and end systolic volume for PN compared to baseline. End systolic volume was also significant compared to propranolol.

Ambulatory Pressures.

Table 40 presents summary of results for 4 patients in PN and 2 propranolol. No analysis was done.

Discussion

Both drugs significantly reduced blood pressures from baseline but the reductions with PN were significantly greater than with propranolol. About 67% propranolol patients were black and this group does not respond as well to beta blockers as do whites. it is possible, therefore, that patient selection may have influenced results in propranol group. There were more ADRs with PN but not serious events requiring withdrawal from study.

Reviewer's Comments

1. This study shows PN to be more effective than propranolol in treatmant of hypertensives. However, as the majority of propranolol patients were black, this could have influenced results

2. Similar comments as previous study with regard to timing of blood pressure measurements

3. PN has a higher incidence of ADRs but more propranolol patients were withdrawn due to ADRs.

TAL
PN 200-110 STUDY NO. 304

DOSAGE SCHEDULE

Treatment Group	Placebo Run-In Weeks -3, -2, -1	Active Treatment+					Optional Tapering Off
		Titration Period			Plateau Period††		
		Weeks 1 & 2++	Weeks 3 & 4++	Weeks 5 & 6++	Weeks 7 & 8	Weeks 9 & 10	
PN 200-110 Group	Pcb* bid	2.5 mg PN 200-110 bid	2.5 mg or 5 mg PN 200-110 bid	2.5 mg, 5 mg or 7.5 mg PN 200-110 bid	2.5 mg, 5 mg 7.5 mg or 10 mg PN 200-110 bid	——→	Taper off
	Total Daily Dose	5 mg	5-10 mg	5-15 mg	5-20 mg	——→	
Propranolol Group	Pcb bid	60 mg Ppnl** bid	60 mg or 120 mg Ppnl bid	60 mg, 120 mg or 180 mg Ppnl bid	60 mg, 120 mg, 180 mg or 240 mg Ppnl bid	——→	Taper off
	Total Daily Dose	120 mg	120-240 mg	120-360 mg	120-480 mg	——→	
	←— Single —→ Blind	←——— Double-Blind ———→					

*Pcb = Placebo
**Ppnl = Propranolol
+Dose of the study drugs was administered bid before breakfast and supper, and at least 30 minutes before the blood pressure was recorded.
++The dose was increased by one capsule (2.5 mg PN 200-110 or 60 mg propranolol) bid at bi-weekly intervals if the sitting diastolic blood pressure was >90 mm Hg at the clinic evaluation. The dose may have been increased any time the average supine diastolic was >110 mm Hg.
††*Beginning with Week 7, the dose of the study drugs remained unchanged.* However, the dose was reduced in a stepwise manner to a lower level in case of an adverse reaction. At no time was the prescribed dose of the study drug to be less than 2.5 mg PN 200-110 bid or 60 mg propranolol bid or to exceed 10 mg PN 200-110 bid or 240 mg propranolol bid.

Table 1

TABLE 2
PFE 200-110 STUDY NO. 304

EVALUATION SCHEDULE

Evaluations	Initial Visit	END OF WEEK													
		Single-Blind			Double-blind: Active Treatment Period										
		Placebo Washout			Titration Period						Plateau Period				12 Follow-up Evaluation
	-4	-3	-2	-1 Time 0	1	2	3	4	5	6	7	8	9	10 Final Evaluations	
Background Information CRF BK, BK-1**	X														
Physical Exam CRF PE	X													X*	
Cardiovascular Evaluation CRF CV	X			X	X	X		X		X		X		X*	
Patient Inclusion/Exclusion Criteria CRF IE				X											
Blood Pressure; Vital Signs CRF VS	X	X	X	X	X	X	X	X	X	X	X	X	X	X*	
24-Hour Ambulatory BP and Heart Rate CRF ABP				X[1]										X*[1]	
Laboratory Evaluation [illegible], urinalysis CBC, chem.) CRF LAB	X			X	X*	X*	X*	X	X*	X	X*	X*	X*	X*	X*
[illegible]aluation CRF ECG	X			X		X		X		X		X		X*	
[illegible]ardiogram CRF EC				X[2]										X*[2]	
Chest X-ray CRF CX	X†													X*	
Ophthalmologic Examination CRF OP				X††										X††	
Concomitant Medication CRF CM	X	- AS REQUIRED -													
Consent CRF CON	X	- AS REQUIRED -													
Medication Check CRF MC		X	X	X	X	X	X	X	X	X	X	X	X	X*	
Adverse Reaction CRF AR		X	X	X	X	X	X	X	X	X	X	X	X	X*	
End of Study Information CRF ES														X	

*Or upon discontinuation from the study.

*Liver function tests only (LDH, SGOT, SGPT, alkaline phosphatase, and total bilirubin) initiated during October/November, 1984.

**Case Report Form identifiers.

†A chest X-ray obtained within six (6) months prior to the patient entering the trial may have served as baseline for the study and was not repeated at the initial visit provided that the chest X-ray was normal and a clinical condition requiring a chest x-ray had not occurred during this interval. Otherwise, a x-ray was obtained.

††The ophthalmologic examination may have been performed any time during the washout period but as close as possible to the week [illegible] 0 visit. The final exam may have been performed within one week of the final evaluations but as close as possible to [illegible]al evaluations.

[illegible]nter C only.

[2]The echocardiogram may have been obtained within 1-4 days prior to the Week -1 and Week 10 clinic visits. This evaluation applies only to Center B.

TABLE 4
PN 200-110 STUDY NO. 304
REASONS FOR PARTIAL VALIDITY OR INVALIDITY FOR EFFICACY ANALYSIS

Patient No.	Treatment Group	Week Discontinued	Valid Thru Week	Reasons
Partially Valid				
204	PN 200-110	4	3	Patient unable to keep appointments
210	PN 200-110	9	8	Uncooperative
216	PN 200-110	8	8	Adverse Reaction - increased angina/shortness of breath
309	PN 200-110	4	3	Emergency Surgery (acute aortic dissection)
~~354~~	~~PN 200-110~~	~~8~~	~~8~~	~~Treatment Failure~~
104	Propranolol	3	3	Adverse Reaction - clouded sensorium
156	Propranolol	3	3	Treatment Failure
158	Propranolol	6	6	Treatment Failure
203	Propranolol	7	6	Subject expired (cardiac arrest secondary to arrhythmia or myocardial infarction).
208	Propranolol	6	5	Uncooperative and Adverse Reaction - abdominal pain
214	Propranolol	7	6	Treatment Failure
313	Propranolol	2	2	Lost to Follow-Up
321	Propranolol	4	4	Adverse Reaction - Fatigue
352	Propranolol	8	6	Adverse Reaction - Gastro-intestinal
353	Propranolol	3	3	Routine Surgery (vaginal)
356	Propranolol	8	7	Adverse Reaction - Fatigue
Invalid				
109*	PN 200-110	N/A	N/A	Non-qualifying blood pressure during washout (diastolic bp <95 mm Hg at Week -1)
308*	PN 200-110	N/A	N/A	Non-qualifying blood pressure during washout (mean diastolic bp 94 mm Hg at Week -2)
319*	PN 200-110	N/A	N/A	Non-compliant - less than 80% medications taken during active treatment
323*	PN 200-110	N/A	N/A	Non-qualifying blood pressure during washout (mean diastolic bp <95 mm Hg at Week -1)
311	Propranolol	1	N/A	Adverse Reaction - Broncho-spasm. Did not take dose of study medication the day of visit.

02

TABLE 5
PN 200-110 STUDY NO. 304

NUMBER OF PATIENTS BY EFFICACY ANALYSES CLASSIFICATION

Investigator	PN 200-110			Propranolol			Total			TOTAL
	Valid	Partially Valid	Invalid	Valid	Partially Valid	Invalid	Valid	Partially Valid	Invalid	
A	13	0	1	11	3	0	24	3	1	28
B	13	3	0	11	3	0	24	6	0	30
C	11	2	3	9	5	1	20	7	4	31
TOTAL	37	5	4	31	11	1	68	16	5	89

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TABLE 7
FN 200-110 STUDY NO. 304

AVERAGE DAILY DOSE (mg) BY STUDY WEEK FOR VALID PATIENTS

Treatment	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
FN 200-110										
N	37	36+	37	37	37	37	36+	37	37	36+
Mean	4.9	4.9	8.3	8.8	10.3	10.7	12.0	11.8	11.8	11.8
S.D.	0.45	0.39	2.43	2.43	3.68	3.92	5.22	5.13	4.94	5.00
Min	3.2	3.8	4.3	4.6	4.3	4.7	4.6	4.3	4.7	5.0
Max	5.8	6.1	11.4	14.4	17.5	18.9	2?.5	20.0	20.0	20.0
Propranolol										
N	31	31	31	31	31	31	31	31	31	31
Mean	118.5	121.9	195.2	197.4	255.2	271.0	332.8	326.3	337.7	329.5
S.D.	6.98	11.84	79.05	61.98	106.83	102.57	144.82	142.16	149.97	145.94
Min	102.9	110.0	100.0	102.9	105.0	102.9	111.4	111.4	111.4	97.5
Max	137.1	180.0	480.0	308.6	531.4	411.4	480.0	480.0	574.3	480.0

+Patient No. 312 failed to return the medication bottles for Weeks 2, 7 and 10 so his average daily dose could not be determined for these time periods.