TABLE 1 (3001)

Summary of Disposition of Randomized Subjects

	Placebo (N=317)	Alosetron 1 mg BID (N=309)	Total (N=626)
Baseline/Week 0			
Assessed	317 (100%)	309 (100%)	626 (100%)
Discontinued	12 (4%)	7 (2%)	19 (3%)
Adverse Event	0	3 (43%)	3 (16%)
Consent Withdrawn	5 (42%)	0	5 (26%)
Lost to Follow up	5 (42%)	4 (57%)	9 (47%)
Protocol Violation	0	0	0
Lack of Efficacy	0	0	0
Other	2 (17%)	0	2 (11%)
Unscheduled			
Assessed	14 (4%)	28 (9%)	42 (7%)
Discontinued	8 (3%)	24 (8%)	32 (5%)
Adverse Event	3 (38%)	19 (79%)	22 (69%)
Consent Withdrawn	1 (13%)	3 (13%)	4 (13%)
Lost to Follow up	0	0	0
Protocol Violation	0	0	0
Lack of Efficacy	1 (13%)	2 (8%)	3 (9%)
Other	3 (38%)	0	3 (9%)
	294 (93%)	[illegible]	
Discontinued	19 (6%)	11 (4%)	30 [illegible]
Adverse Event	5 (26%)	7 (64%)	12 (40%)
Consent Withdrawn	9 (47%)	0	9 (30%)
Lost to Follow up	4 (21%)	1 (9%)	5 (17%)
Protocol Violation	0	1 (9%)	1 (3%)
Lack of Efficacy	1 (5%)	2 (18%)	3 (10%)
Other	0	0	0
Unscheduled			
Assessed	18 (6%)	19 (6%)	37 (6%)
Discontinued	11 (3%)	12 (4%)	23 (4%)
Adverse Event	5 (45%)	8 (67%)	13 (57%)
Consent Withdrawn	5 (45%)	1 (8%)	6 (26%)
Lost to Follow up	0	0	0
Protocol Violation	0	0	0
Lack of Efficacy	1 (9%)	1 (8%)	2 (9%)
Other	0	2 (17%)	2 (9%)
Week 8			
Assessed	267 (84%)	254 (82%)	521 (83%)
Discontinued	12 (4%)	13 (4%)	25 (4%)
Adverse Event	4 (33%)	9 (69%)	13 (52%)
Consent Withdrawn	3 (25%)	1 (8%)	4 (16%)
Lost to Follow up	0	1 (8%)	1 (4%)
Protocol Violation	0	0	0
Lack of Efficacy	4 (33%)	2 (15%)	6 (24%)
Other	1 (8%)	0	1 (4%)
Unscheduled			
Assessed	5 (2%)	9 (3%)	14 (2%)
Discontinued	1 (<1%)	2 (<1%)	3 (<1%)
Adverse Event	1 (100%)	0	1 (33%)
Consent Withdrawn	0	0	0
Lost to Follow up	0	0	0
Protocol Violation	0	0	0
Lack of Efficacy	0	0	0
Other	0	2 (100%)	2 (67%)
Week 12			
Assessed	253 (80%)	238 (77%)	491 (78%)
Discontinued	7 (2%)	1 (<1%)	8 (1%)
Adverse Event	2 (29%)	0	2 (25%)
Consent Withdrawn	2 (29%)	1 (100%)	3 (38%)
Lost to Follow up	2 (29%)	0	2 (25%)
Protocol Violation	0	0	0
Lack of Efficacy	0	0	0
Other	1 (14%)	0	1 (13%)
Unscheduled			
Assessed	5 (2%)	9 (3%)	14 (2%)
Discontinued	0	0	0
Adverse Event	0	0	0
Consent Withdrawn	0	0	0
Lost to Follow up	0	0	0
Protocol Violation	0	0	0
Lack of Efficacy	0	0	0
Other	0	0	0

TABLE 2 (3002)

Summary of Disposition of Randomized Subjects

	Placebo (N=323)	Alosetron 1 mg BID (N=324)	Total (N=647)
Baseline/Week 0			
Assessed	323 (100%)	324 (100%)	647 (100%)
Discontinued	6 (2%)	12 (4%)	18 (3%)
Adverse Event	1 (17%)	2 (17%)	3 (17%)
Consent Withdrawn	1 (17%)	4 (33%)	5 (28%)
Lost to Follow up	3 (50%)	6 (50%)	9 (50%)
Protocol Violation	0	0	0
Lack of Efficacy	1 (17%)	0	1 (6%)
Other	0	0	0
Unscheduled			
Assessed	12 (4%)	13 (4%)	25 (4%)
Discontinued	7 (2%)	12 (4%)	19 (3%)
Adverse Event	4 (57%)	10 (83%)	14 (74%)
Consent Withdrawn	3 (43%)	1 (8%)	4 (21%)
Lost to Follow up	0	0	0
Protocol Violation	0	0	0
Lack of Efficacy	0	1 (8%)	1 (5%)
Other	0	0	0
Week 4			
Assessed	310 (96%)	300 (93%)	610 (94%)
Discontinued	17 (5%)	28 (9%)	45 (7%)
Adverse Event	4 (24%)	22 (79%)	26 (58%)
Consent Withdrawn	3 (18%)	2 (7%)	5 (11%)
Lost to Follow up	3 (18%)	1 (4%)	4 (9%)
Protocol Violation	0	1 (4%)	1 (2%)
Lack of Efficacy	6 (35%)	2 (7%)	8 (18%)
Other	1 (6%)	0	1 (2%)
Unscheduled			
Assessed	15 (5%)	7 (2%)	22 (3%)
Discontinued	4 (1%)	3 (<1%)	7 (1%)
Adverse Event	0	2 (67%)	2 (29%)
Consent Withdrawn	0	0	0
Lost to Follow up	0	0	0
Protocol Violation	1 (25%)	0	1 (14%)
Lack of Efficacy	3 (75%)	1 (33%)	4 (57%)
Other	0	0	0
Week 8			
Assessed	288 (89%)	269 (83%)	557 (86%)
Discontinued	8 (2%)	13 (4%)	21 (3%)
Adverse Event	3 (38%)	8 (62%)	11 (52%)
Consent Withdrawn	1 (13%)	1 (8%)	2 (10%)
Lost to Follow up	1 (13%)	2 (15%)	3 (14%)
Protocol Violation	0	0	0
Lack of Efficacy	3 (38%)	1 (8%)	4 (19%)
Other	0	1 (8%)	1 (5%)
Unscheduled			
Assessed	13 (4%)	8 (2%)	21 (3%)
Discontinued	3 (<1%)	2 (<1%)	5 (<1%)
Adverse Event	0	1 (50%)	1 (20%)
Consent Withdrawn	0	1 (50%)	1 (20%)
Lost to Follow up	0	0	0
Protocol Violation	1 (33%)	0	1 (20%)
Lack of Efficacy	1 (33%)	0	1 (20%)
Other	1 (33%)	0	1 (20%)
Week 12			
Assessed	278 (86%)	253 (78%)	531 (82%)
Discontinued	8 (2%)	8 (2%)	16 (2%)
Adverse Event	2 (25%)	3 (38%)	5 (31%)
Consent Withdrawn	0	1 (13%)	1 (6%)
Lost to Follow up	4 (50%)	2 (25%)	6 (38%)
Protocol Violation	0	0	0
Lack of Efficacy	0	1 (13%)	1 (6%)
Other	2 (25%)	1 (13%)	3 (19%)
Unscheduled			
Assessed	8 (2%)	5 (2%)	13 (2%)
Discontinued	0	1 (<1%)	1 (<1%)
Adverse Event	0	1 (100%)	1 (100%)
Consent Withdrawn	0	0	0
Lost to Follow up	0	0	0
Protocol Violation	0	0	0
Lack of Efficacy			

TABLE 3 (_ _)

Monthly Adequate Relief of IBS Pain/Discomfort: ITT

Measurement	Statistic	Placebo (N=317)	Alosetron 1 mg BID (N=309)	Treatment Difference	95% CI for Treatment Difference	p-value
3a-ITT						
Number of Adequate Relief Responders						
Month 1	n (%) (95% CI)	126 (40%) (34.4%,45.1%)	154 (50%) (44.3%,55.4%)	10.1%	(2.3%,17.8%)	0.010*
Month 2	n (%) (95% CI)	137 (43%) (37.8%,48.7%)	176 (57%) (51.4%,62.5%)	13.7%	(6.0%,21.5%)	<0.001*
Month 3	n (%) (95% CI)	130 (41%) (35.6%,46.4%)	179 (58%) (52.4%,63.4%)	16.9%	(9.2%,24.6%)	<0.001*

Measurement	Statistic	Placebo (N=222)	Alosetron 1 mg BID (N=224)	Treatment Difference	95% CI for Treatment Difference	p-value
3b-D-IBS						
Number of Adequate Relief Responders						
Month 1	n (%) (95% CI)	87 (39%) (32.8%,45.6%)	112 (50%) (43.5%,56.5%)	10.8%	(1.6%,20.0%)	0.022*
Month 2	n (%) (95% CI)	96 (43%) (36.7%,49.8%)	129 (58%) (51.1%,64.1%)	14.3%	(5.2%,23.5%)	0.003*
Month 3	n (%) (95% CI)	92 (41%) (35.0%,47.9%)	135 (60%) (53.9%,66.7%)	18.8%	(9.7%,27.9%)	<0.001*

Measurement	Statistic	Placebo (N=87)	Alosetron 1 mg BID (N=82)	Treatment Difference	95% CI for Treatment Difference	p-valu
3c-A-IBS						
Number of Adequate Relief Responders						
Month 1	n (%) (95% CI)	36 (41%) (31.0%,51.7%)	40 (49%) (38.0%,59.6%)	7.4%	(-7.6%,22.4%)	0.29
Month 2	n (%) (95% CI)	38 (44%) (33.3%,54.1%)	45 (55%) (44.1%,65.6%)	11.2%	(-3.8%,26.2%)	0.12
Month 3	n (%) (95% CI)	37 (43%) (32.1%,52.9%)	42 (51%) (40.4%,62.0%)	8.7%	(-8.3%,23.7%)	0.22

Note: A subject is defined as a responder if they report adequate relief of abdominal pain/discomfort for at least two of the four weeks during a month.

Note: P-values are the result of a Mantel-Haenszel test with stratification for cluster

Monthly Adequate Relie IS Pain/Discomfort: LOCF

TABLE 4

4a-ITT

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)	Treatment Difference	95% CI for Treatment Difference	p-value
Number of Adequate Relief Responders						
Month 1	n (%) (95% CI)	137 (42%) (37.0%,47.8%)	169 (52%) (46.7%,57.6%)	9.7%	(2.1%,17.4%)	0.019*
Month 2	n (%) (95% CI)	152 (47%) (41.6%,52.5%)	176 (54%) (48.9%,59.7%)	7.3%	(-0.4%,14.9%)	0.080
Month 3	n (%) (95% CI)	151 (47%) (41.3%,52.2%)	183 (56%) (51.1%,61.9%)	9.7%	(2.1%,17.4%)	0.015*

4b-D-IBS

Measurement	Statistic	Placebo (N=221)	Alosetron 1 mg BID (N=237)	Treatment Difference	95% CI for Treatment Difference	p-value
Number of Adequate Relief Responders						
Month 1	n (%) (95% CI)	89 (40%) (33.8%,46.7%)	139 (59%) (52.4%,64.9%)	18.4%	(9.4%,27.4%)	<0.001**
Month 2	n (%) (95% CI)	104 (47%) (40.5%,53.6%)	140 (59%) (52.8%,65.3%)	12.0%	(2.9%,21.1%)	0.013*
Month 3	n (%) (95% CI)	100 (45%) (38.7%,51.8%)	145 (61%) (55.0%,67.4%)	15.9%	(6.9%,25.0%)	<0.001**

4c_A-IBS

Measurement	Statistic	Placebo (N=95)	Alosetron 1 mg BID (N=85)	Treatment Difference	95% CI for Treatment Difference	p-value
Number of Adequate Relief Responders						
Month 1	n (%) (95% CI)	45 (47%) (37.3%,57.4%)	29 (34%) (24.0%,44.2%)	-13.3%	(-27.5%,1.0%)	0.058
Month 2	n (%) (95% CI)	46 (48%) (38.4%,58.5%)	35 (41%) (30.7%,51.6%)	-7.2%	(-21.8%,7.3%)	0.356
Month 3	n (%) (95% CI)	48 (51%) (40.5%,60.6%)	36 (42%) (31.8%,52.9%)	-8.2%	(-22.7%,6.4%)	0.289

Note: A subject is defined as a responder if they report adequate relief of abdominal pain/discomfort for at least two of the four weeks during a month.

Note: P-values are the result of a Mantel-Haenszel test with stratification for cluster.

Number of Months with Adequate Relief of IBS Pain/Discomfort: LOCF

Measurement	Statistic	Placebo (N=317)	Alosetron 1 mg BID (N=309)	p-value
Number of Months Subject is an Adequate Relief Responder	n (%)			
0		135 (43%)	100 (32%)	<0.001**
1		53 (17%)	36 (12%)	
2		47 (15%)	46 (15%)	
3		82 (26%)	127 (41%)	
IBS Subtype: Diarrhea-predominant	n	222	224	
Number of Months Subject is an Adequate Relief Responder	n (%)			<0.001**
0		95 (43%)	71 (32%)	
1		37 (17%)	26 (12%)	
2		32 (14%)	31 (14%)	
3		58 (26%)	96 (43%)	
IBS Subtype: Alternating Constipation and Diarrhea	n	87	82	
Number of Months Subject is an Adequate Relief Responder	n (%)			0.133
0		35 (40%)	28 (34%)	
1		16 (18%)	10 (12%)	
2		13 (15%)	15 (18%)	
3		23 (26%)	29 (35%)	

TABLE 5 (3001)

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: Percentages are based on the number of subjects with each IBS subtype.
Note: A subject is defined as a responder if they report adequate relief of abdominal pain/discomfort for at least two of the four weeks during a month.
Note: P-values are the result of a Cochran-Mantel-Haenszel test with integer scores and stratification for cluster.

Number of Months with Adequate Relief of IBS Pain/Discomfort: LOCF

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)	p-value
Number of Months Subject is an Adequate Relief Responder	n (%)			0.012*
0		129 (40%)	108 (33%)	
1		42 (13%)	37 (11%)	
2		58 (18%)	46 (14%)	
3		94 (29%)	133 (41%)	

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)	p-value
IBS Subtype: Diarrhea-predominant	n	221	237	
Number of Months Subject is an Adequate Relief Responder	n (%)			<0.001**
0		90 (41%)	67 (28%)	
1		31 (14%)	26 (11%)	
2		38 (17%)	34 (14%)	
3		62 (28%)	110 (46%)	
IBS Subtype: Alternating Constipation and Diarrhea	n	95	85	
Number of Months Subject is an Adequate Relief Responder	n (%)			0.131
0		35 (37%)	41 (48%)	
1		11 (12%)	10 (12%)	
2		19 (20%)	12 (14%)	
3		30 (32%)	22 (26%)	

TABLE 6 (3002)

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: Percentages are based on the number of subjects with each IBS subtype.
Note: A subject is defined as a responder if they report adequate relief of abdominal pain/discomfort for at least two of the four weeks during a month.
Note: P-values are the result of a Cochran-Mantel-Haenszel test with integer scores and stratification for cluster.

TABLE 7

Summary of Correlation Between Adequate Relief Response and Average Pain Severity By Week and Overall

Time	N	Adequate Relief Responder	n (%)	Baseline Mean	Baseline SD	Change from Baseline Mean	Change from Baseline SD	Spearman Rank Correlation Coefficient	p-value
Week 1	594	Yes	187 (31%)	1.8	0.6	-0.7	0.7	-0.344	<0.001**
		No	407 (69%)	2.0	0.6	-0.1	0.6		
Week 2	576	Yes	227 (39%)	1.9	0.6	-1.0	0.8	-0.486	<0.001**
		No	349 (61%)	2.0	0.6	-0.2	0.7		
Week 3	569	Yes	268 (47%)	1.9	0.6	-1.0	0.8	-0.399	<0.001**
		No	301 (53%)	2.0	0.6	-0.4	0.7		
Week 4	553	Yes	253 (46%)	1.9	0.6	-1.1	0.7	-0.480	<0.001**
		No	300 (54%)	2.0	0.6	-0.4	0.7		
Week 5	538	Yes	277 (51%)	1.9	0.6	-1.2	0.7	-0.418	<0.001**
		No	261 (49%)	2.0	0.6	-0.5	0.8		
Week 6	528	Yes	268 (51%)	1.9	0.6	-1.2	0.7	-0.421	<0.001**
		No	260 (49%)	2.0	0.6	-0.5	0.8		
Week 7	518	Yes	248 (48%)	1.9	0.6	-1.2	0.7	-0.455	<0.001**
		No	270 (52%)	2.0	0.6	-0.5	0.7		
Week 8	510	Yes	272 (53%)	1.9	0.6	-1.3	0.7	-0.495	<0.001**
		No	238 (47%)	2.0	0.6	-0.5	0.8		
Week 9	496	Yes	263 (53%)	1.9	0.6	-1.3	0.7	-0.454	<0.001**
		No	233 (47%)	2.0	0.6	-0.6	0.7		
Week 10	486	Yes	254 (52%)	1.9	0.6	-1.3	0.7	-0.467	<0.001**
		No	232 (48%)	2.0	0.6	-0.6	0.7		
Week 11	481	Yes	238 (49%)	1.9	0.6	-1.3	0.7	-0.431	<0.001**
		No	243 (51%)	2.0	0.6	-0.6	0.7		
Week 12	463	Yes	242 (52%)	1.9	0.6	-1.2	0.8	-0.403	<0.001**
		No	221 (48%)	2.0	0.6	-0.6	0.8		
At least Six out of Twelve Weeks	483	Yes	254 (53%)	1.9	0.6	-1.1	0.6	-0.455	<0.001**
		No	229 (47%)	2.0	0.6	-0.5	0.5		

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: For each week, subjects who answered the adequate relief question and who answered the pain/discomfort question on at least one day are included in the analysis at that week. The analysis of subjects who reported adequate relief in at least six out of twelve weeks is based on the number of subjects who completed the study.
Note: P-values are the result of a Wilcoxon rank-sum test for comparison of the adequate relief Yes/No response groups.

TABLE 8

Proportion of Weeks with Adequate Relief
By Whether the Week Overlapped Menstruation

8a (3001)

Measurement	Statistic	Placebo (N=317)	Alosetron 1 mg BID (N=309)	Between Treatment Group Comparison p-value [1]
Proportion of weeks with adequate relief overlapping with menstrual cycle	n	117	118	<0.001**
	Mean	0.38	0.62	
	SD	0.39	0.39	
	Median	0.33	0.71	
	Min.	0.0	0.0	
	Max.	1.0	1.0	
Proportion of weeks with adequate relief not overlapping with menstrual cycle	n	128	127	<0.001**
	Mean	0.37	0.57	
	SD	0.36	0.37	
	Median	0.33	0.67	
	Min.	0.0	0.0	
	Max.	1.0	1.0	
Within treatment group comparison [2]	p-value	0.541	0.243	

8b (3002)

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)	Between Treatment Group Comparison p-value [1]
Proportion of weeks with adequate relief overlapping with menstrual cycle	n	119	122	<0.001**
	Mean	0.39	0.58	
	SD	0.39	0.40	
	Median	0.25	0.67	
	Min.	0.0	0.0	
	Max.	1.0	1.0	
Proportion of weeks with adequate relief not overlapping with menstrual cycle	n	126	128	<0.001**
	Mean	0.37	0.53	
	SD	0.37	0.39	
	Median	0.25	0.56	
	Min.	0.0	0.0	
	Max.	1.0	1.0	
Within treatment group comparison [2]	p-value	0.273	0.067	

* Significant at the 0.050 level; ** significant at the 0.010 level.

Note: Subjects who menstruated during the study are included in the table. The proportion of weeks with adequate relief overlapping the menstrual cycle was calculated for subjects who answered the adequate relief question during at least one week that overlapped the menstrual cycle. The proportion of weeks with adequate relief not overalapping with menstrual cycle was calculated for subjects who answered the adequate relief question during at least one week that did not overlap the menstrual cycle.

[1] P-values are the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

[2] P-values for the difference in proportion of weeks with adequate relief overlapping with menstrual cycle and the proportion of weeks with adequate relief not overlapping with menstrual cycle are the result of the Wilcoxon signed rank test.

FIGURE 1 (...)

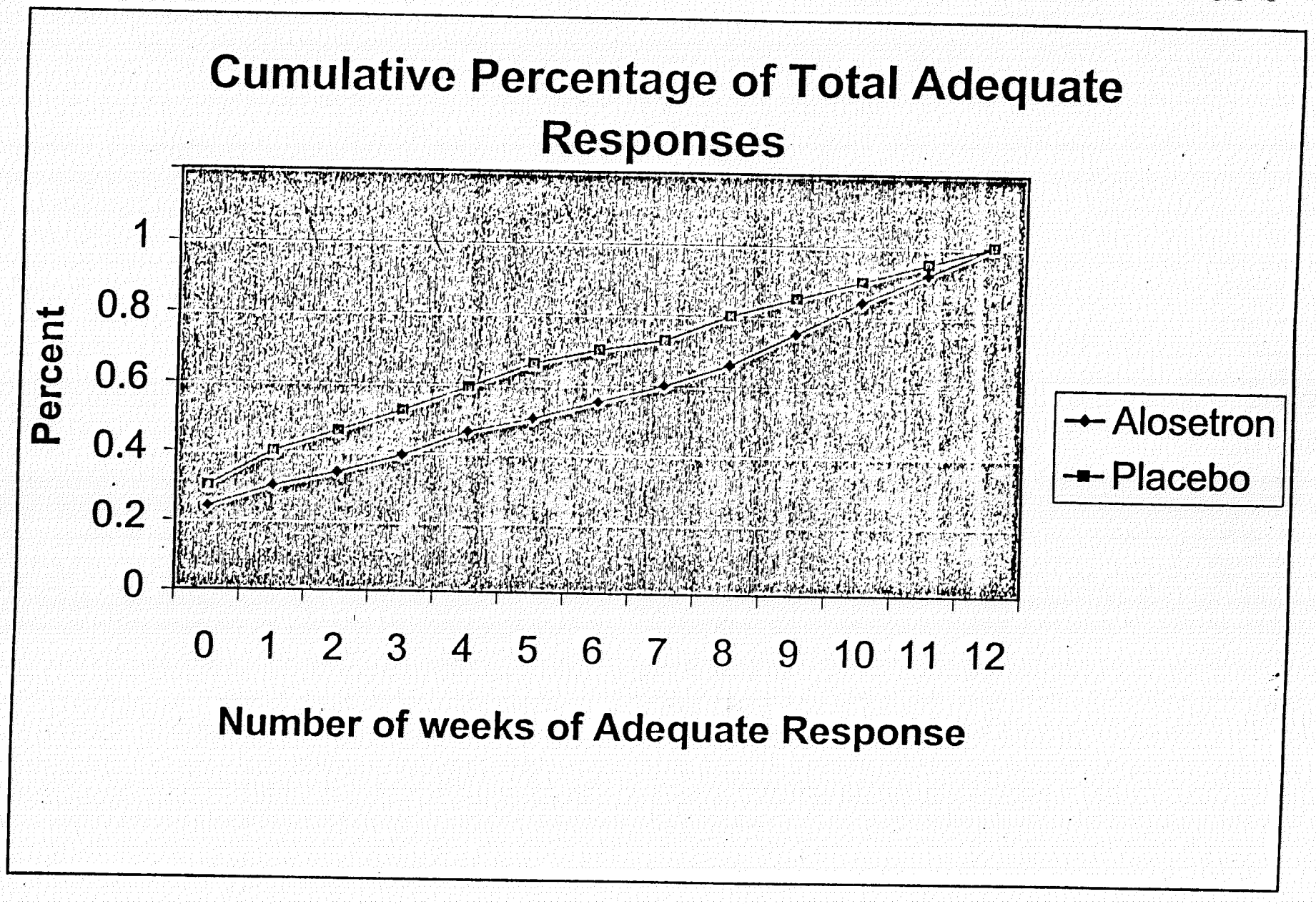

FIGURE 2

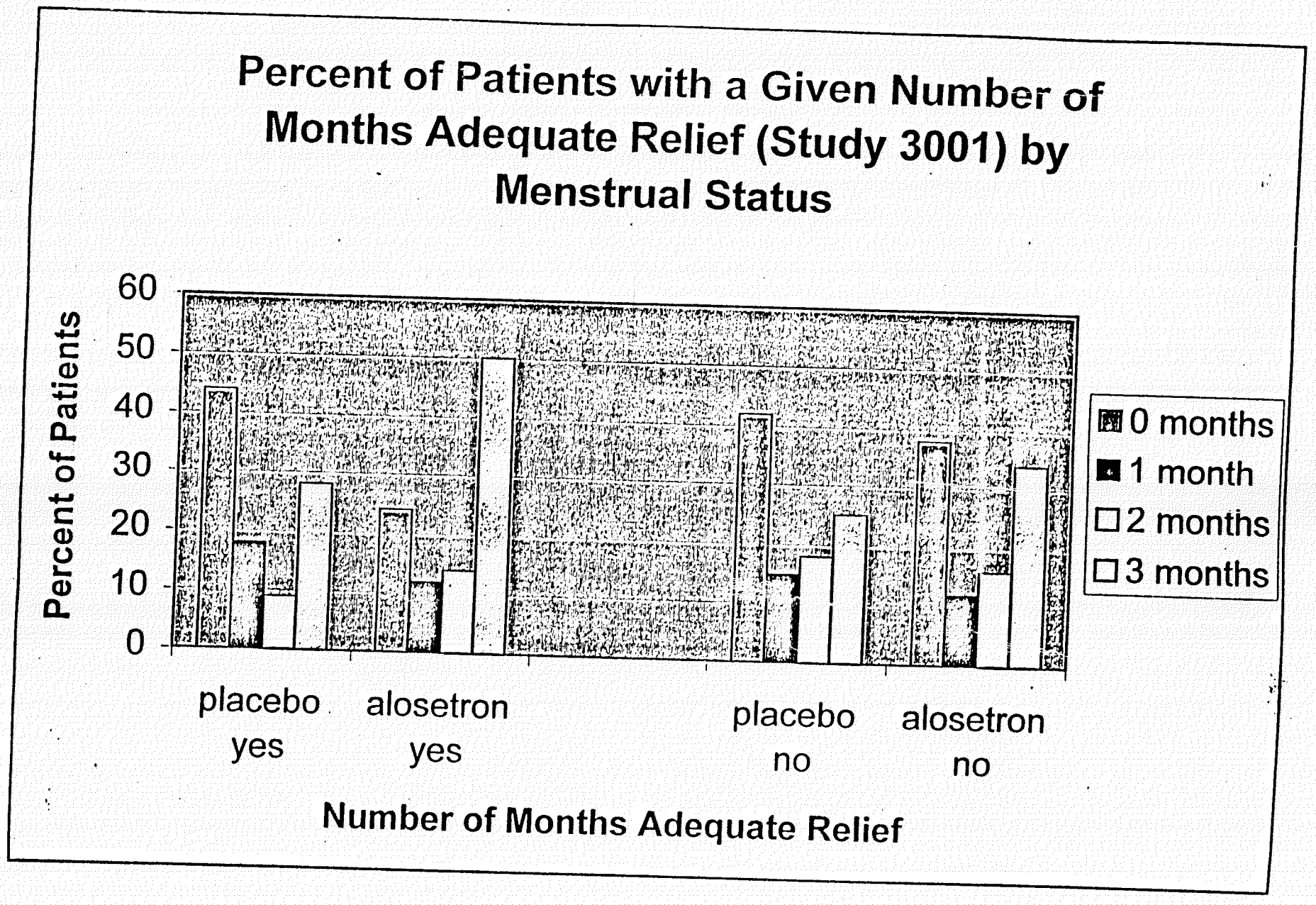

FIGURE 3 (30

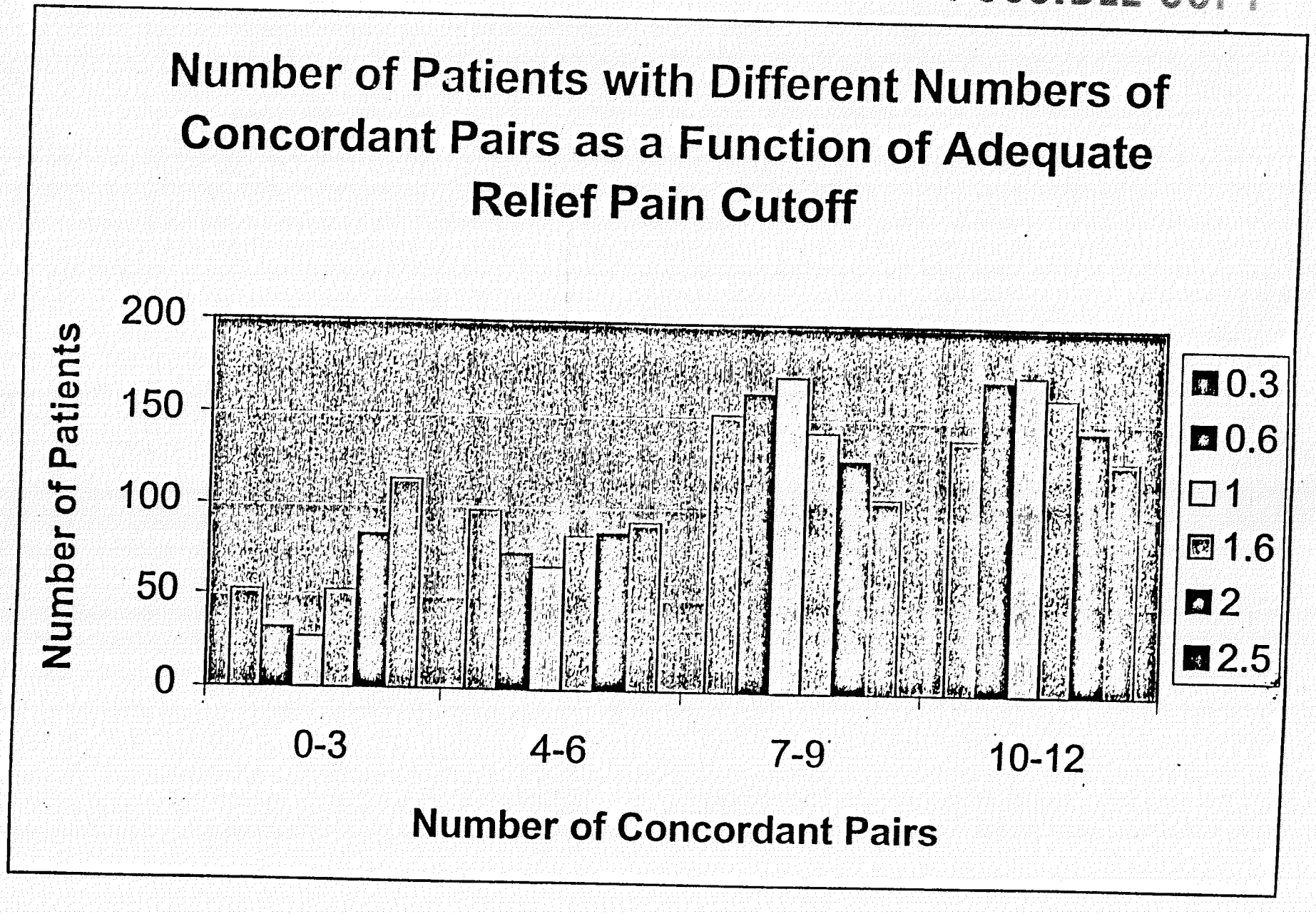

FIGURE 4 (p. ..ed 3001 & 3002)