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Protocol: S3BA3001
Population: ITT (Diarrhea-Predominant)

Table D-7.34
Monthly Abdominal Pain/Discomfort Scores
LOCF

Measurement	Statistic	Placebo (N=222)	Alosetron 1 mg BID (N=224)
Pain/Discomfort Score			
Baseline			
	n	222	224
	Mean	1.97	1.85
	SD	0.60	0.57
	Median	1.92	1.79
	Min.		
	Max.		
Month 1			
	n	222	224
	Mean	1.40	1.33
	SD	0.74	0.65
	Median	1.26	1.30
	Min.		
	Max.		
Month 2			
	n	222	224
	Mean	1.24	1.07
	SD	0.81	0.74
	Median	1.14	0.94
	Min.		
	Max.		

Note: Low scores are favored for abdominal pain/discomfort; 0 - none, 1 - mild, 2 - moderate, 3 - intense, 4 - severe pain/discomfort.
Note: LOCF - last observation carried forward.

Source: ALOS050DEV:[S3BA3001.TABLELIB.IBSDP]DP_ITT_ABDPAIN_MW.SAS/QUINTILES (US)/16APR99/11:16

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Protocol: S38A3001
Population: ITT (Diarrhea-Predominant)

Table D-7.34
Monthly Abdominal Pain/Discomfort Scores
LOCF

Measurement	Statistic	Placebo (N=222)	Alosetron 1 mg BID (N=224)
Pain/Discomfort Score			
Month 3	n	222	224
	Mean	1.24	1.00
	SD	0.84	0.78
	Median	1.12	0.82
	Min.		
	Max.		

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Protocol: S3BA3001
Population: ITT (Alternating)

Table A-7.34
Monthly Abdominal Pain/Discomfort Scores
LOCF

Measurement	Statistic	Placebo (N=87)	Alosetron 1 mg BID (N=82)
Pain/Discomfort Score			
Baseline	n	87	82
	Mean	1.99	2.13
	SD	0.62	0.61
	Median	2.00	2.11
	Min.		
	Max.		
Month 1	n	87	82
	Mean	1.53	1.60
	SD	0.79	0.78
	Median	1.41	1.50
	Min.		
	Max.		
Month 2	n	87	82
	Mean	1.31	1.33
	SD	0.80	0.81
	Median	1.20	1.21
	Min.		
	Max.		

Note: Low scores are favored for abdominal pain/discomfort; 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.

Source: ALOS0500EV:[S3BA3001.TABLELIB.IBSACD]ACD_ITT_ABDPAIN_MM.SAS/QUINTILES (US)/18APR99/18:35

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Protocol: S3BA3001
Population: ITT (Alternating)

Table A-7.34
Monthly Abdominal Pain/Discomfort Scores
LOCF

Measurement	Statistic	Placebo (N=87)	Alosetron 1 mg BID (N=82)
Pain/Discomfort Score Month 3	n	87	82
	Mean	1.26	1.19
	SD	0.80	0.88
	Median	1.07	1.08
	Min.		
	Max.		

Note: Low scores are favored for abdominal pain/discomfort; 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.

Source: ALOS050DEV:[S3BA3001.TABLELIB.IBSACD]ACD_ITT_ABDPAIN_MN.SAS/QUINTILES (US)/18APR99/16:35

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Protocol: S3BA3001
Population: Intent-to-Treat

Table T-7.35
Monthly Abdominal Pain/Discomfort Scores
Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=317)	Alosetron 1 mg BID (N=309)	p-value
Change in Pain/Discomfort Score Month 1	n	317	309	0.869
	Mean	-0.54	-0.52	
	SD	0.64	0.67	
	Median	-0.47	-0.46	
	Min.			
	Max.			
Month 2	n	317	309	0.126
	Mean	-0.70	-0.79	
	SD	0.73	0.77	
	Median	-0.73	-0.82	
	Min.			
	Max.			
Month 3	n	317	309	0.014*
	Mean	-0.72	-0.86	
	SD	0.78	0.83	
	Median	-0.76	-0.89	
	Min.			
	Max.			

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: Low scores are favored for abdominal pain/discomfort; 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOS050DEV:[S3BA3001.TABLELIB]ITT_ABDPAIN_MNTHLY_CFB.SAS/QUINTILES (US)/15APR99/10:54

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Protocol: S3BA3001
Population: ITT (Diarrhea-Predominant)

Table 0-7.35
Monthly Abdominal Pain/Discomfort Scores
Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=222)	Alosetron 1 mg BID (N=224)	p-value
Change in Pain/Discomfort Score				
Month 1	n	222	224	0.407
	Mean	-0.58	-0.52	
	SD	0.64	0.67	
	Median	-0.49	-0.47	
	Min.			
	Max.			
Month 2	n	222	224	0.546
	Mean	-0.73	-0.78	
	SD	0.75	0.77	
	Median	-0.78	-0.80	
	Min.			
	Max.			
Month 3	n	222	224	0.160
	Mean	-0.73	-0.85	
	SD	0.79	0.83	
	Median	-0.75	-0.86	
	Min.			
	Max.			

Note: Low scores are favored for abdominal pain/discomfort: 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOS050DEV:[S3BA3001.TABLELIB.IBSDP]DP_ITT_ABDPAIN_MC.SAS/QUINTILES (US)/16APR99/11:18

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Protocol: S3BA3001
Population: ITT (Alternating)

Table A-7.35
Monthly Abdominal Pain/Discomfort Scores
Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=87)	Alosetron 1 mg BID (N=82)	p-value
Change in Pain/Discomfort Score				
Month 1	n	87	82	0.397
	Mean	-0.46	-0.53	
	SD	0.61	0.69	
	Median	-0.41	-0.46	
	Min.			
	Max.			
Month 2	n	87	82	0.121
	Mean	-0.88	-0.80	
	SD	0.88	0.79	
	Median	-0.69	-0.84	
	Min.			
	Max.			
Month 3	n	87	82	0.034*
	Mean	-0.73	-0.94	
	SD	0.66	0.84	
	Median	-0.77	-0.90	
	Min.			
	Max.			

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: Low scores are favored for abdominal pain/discomfort: 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOSO50DEV:[S3BA3001.TABLEL18.IBSACO]ACO_ITT_ABDPAIN_MC.SAS/QUINTILES (US)/18APR99/16:36

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APPENDIX 5

Fibromyalgia Subset (A3002)

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Protocols: S3BA3001 and S3BA3002
Population: Intent-to-Treat (Subjects Consenting to Genetic Sampling)

Table T-1
Weekly Adequate Relief of IBS Pain/Discomfort: LOCF

	Placebo	Placebo	Alosetron 1mg BID	Alosetron 1mg BID
	No Fibromyalgia (N=118)	Fibromyalgia (N=13)	No Fibromyalgia (N=106)	Fibromyalgia (N=12)
Number of Subjects with Adequate Relief During the Treatment Phase				
Week 1	34 (29%)	7 (54%)	44 (42%)	4 (33%)
Week 2	52 (44%)	4 (31%)	58 (55%)	7 (58%)
Week 3	48 (41%)	4 (31%)	60 (57%)	8 (67%)
Week 4	44 (37%)	4 (31%)	65 (61%)	7 (58%)
Week 5	57 (48%)	3 (23%)	68 (64%)	7 (58%)
Week 6	56 (47%)	4 (31%)	69 (65%)	8 (67%)
Week 7	61 (52%)	4 (31%)	63 (59%)	8 (67%)
Week 8	58 (49%)	5 (38%)	66 (62%)	8 (67%)
Week 9	56 (47%)	7 (54%)	73 (69%)	8 (67%)
Week 10	53 (45%)	4 (31%)	68 (64%)	8 (67%)
Week 11	47 (40%)	3 (23%)	63 (59%)	8 (67%)
Week 12	46 (39%)	4 (31%)	74 (70%)	6 (50%)
Number of Subjects with Adequate Relief During the Follow-up Phase				
Week 1	35 (30%)	2 (15%)	48 (45%)	1 (8%)
Week 2	40 (34%)	1 (8%)	29 (27%)	1 (8%)
Week 3	25 (21%)	1 (8%)	31 (29%)	2 (17%)
Week 4	21 (18%)	1 (8%)	25 (24%)	1 (8%)

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Protocols: S3BA3001 and S3BA3002
Population: ITT (Diarrhea-Predominant: Subjects Consenting to Genetic Sampling)

Table D-1
Weekly Adequate Relief of IBS Pain/Discomfort: *LOCF*

	Placebo	Placebo	Alosetron 1mg BID	Alosetron 1mg BID
	No Fibromyalgia (N=88)	Fibromyalgia (N=6)	No Fibromyalgia (N=79)	Fibromyalgia (N=10)
Number of Subjects with Adequate Relief During the Treatment Phase				
Week 1	24 (27%)	2 (33%)	34 (43%)	3 (30%)
Week 2	37 (42%)	1 (17%)	48 (61%)	7 (70%)
Week 3	34 (39%)	1 (17%)	45 (57%)	6 (60%)
Week 4	32 (36%)	1 (17%)	51 (65%)	6 (60%)
Week 5	41 (47%)	0	54 (68%)	6 (60%)
Week 6	39 (44%)	2 (33%)	54 (68%)	7 (70%)
Week 7	45 (51%)	1 (17%)	48 (61%)	7 (70%)
Week 8	42 (48%)	3 (50%)	51 (65%)	7 (70%)
Week 9	40 (45%)	4 (67%)	57 (72%)	6 (60%)
Week 10	38 (43%)	2 (33%)	53 (67%)	6 (60%)
Week 11	34 (39%)	1 (17%)	48 (61%)	7 (70%)
Week 12	32 (36%)	2 (33%)	56 (71%)	6 (60%)
Number of Subjects with Adequate Relief During the Follow-up Phase				
Week 1	24 (27%)	2 (33%)	38 (48%)	1 (10%)
Week 2	25 (28%)	1 (17%)	21 (27%)	1 (10%)
Week 3	18 (20%)	1 (17%)	24 (30%)	2 (20%)
Week 4	14 (16%)	1 (17%)	18 (23%)	1 (10%)

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APPENDIX 6

Trial A3002. Patient Rating of Abdominal Pain/Discomfort

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Protocol: S3BA3002
Population: Intent-to-Treat

Table T-7.34
Monthly Abdominal Pain/Discomfort Scores
LOCF

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)
Pain/Discomfort Score Baseline	n	323	324
	Mean	1.90	1.95
	SD	0.63	0.60
	Median	1.77	1.95
	Min.		
	Max.		
Month 1	n	323	324
	Mean	1.34	1.39
	SD	0.73	0.73
	Median	1.26	1.33
	Min.		
	Max.		
Month 2	n	323	324
	Mean	1.18	1.12
	SD	0.82	0.77
	Median	1.04	1.00
	Min.		
	Max.		

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Protocol: S3BA3002
Population: Intent-to-Treat

Table T-7.34
Monthly Abdominal Pain/Discomfort Scores
LOCF

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)
Pain/Discomfort Score Month 3	n	323	324
	Mean	1.17	1.08
	SD	0.88	0.84
	Median	1.00	0.90
	Min.		
	Max.		

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Protocol: S3BA3002
Population: Intent-to-Treat

Table T-7.35
Monthly Abdominal Pain/Discomfort Scores
Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=323)	Alosetron 1 mg BID (N=324)	p-value
Change in Pain/Discomfort Score Month 1	n	323	324	0.840
	Mean	-0.55	-0.56	
	SD	0.81	0.71	
	Median	-0.50	-0.55	
	Min.			
	Max.			
Month 2	n	323	324	0.020*
	Mean	-0.72	-0.83	
	SD	0.75	0.80	
	Median	-0.68	-0.87	
	Min.			
	Max.			
Month 3	n	323	324	0.036*
	Mean	-0.73	-0.87	
	SD	0.83	0.86	
	Median	-0.69	-0.86	
	Min.			
	Max.			

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: Low scores are favored for abdominal pain/discomfort; 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOS050DEV:[S3BA3002.TABLELIB]ITT_ABDPAIN_MNTHLY_CFB.SAS/QUINTILES (US)/30MAR99/21:59

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Protocol: S3BA3002
Population: ITT (Diarrhea-Predominant)

Table D-7.35
Monthly Abdominal Pain/Discomfort Scores
Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=221)	Alosetron 1 mg BID (N=237)	p-value
Change in Pain/Discomfort Score				
Month 1	n	221	237	0.121
	Mean	-0.57	-0.68	
	SD	0.63	0.71	
	Median	-0.50	-0.62	
	Min.			
	Max.			
Month 2	n	221	237	0.005**
	Mean	-0.74	-0.92	
	SD	0.79	0.79	
	Median	-0.70	-0.83	
	Min.			
	Max.			
Month 3	n	221	237	0.012*
	Mean	-0.75	-0.96	
	SD	0.87	0.85	
	Median	-0.75	-0.92	
	Min.			
	Max.			

* significant at the 0.050 level; ** significant at the 0.010 level.
Note: Low scores are favored for abdominal pain/discomfort; 0 = none, 1 = mild, 2 = moderate, 3 = intense, 4 = severe pain/discomfort.
Note: LOCF = last observation carried forward.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOS0500EV:[S3BA3002.TABLELIB.IBSDP]DP_ITT_ABDPAIN_MC.SAS/QUINTILES (US)/31MAR99/13:49

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APPENDIX 7

Trial A3002. Stool Consistency

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Protocol: S3BA3002
Population: ITT (Diarrhea-Predominant)

Table D-7.42
Lower GI Parameters: Stool Consistency
By Month: LOCF

Measurement	Statistic	Placebo (N=221)	Alosetron 1 mg BID (N=237)
Stool Consistency			
Baseline	n	221	237
	Mean	3.57	3.55
	SD	0.55	0.50
	Median	3.62	3.57
	Min.		
	Max.		
Month 1	n	221	237
	Mean	3.28	2.52
	SD	0.61	0.82
	Median	3.27	2.55
	Min.		
	Max.		
Month 2	n	221	237
	Mean	3.27	2.52
	SD	0.59	0.82
	Median	3.28	2.58
	Min.		
	Max.		
Month 3	n	221	237
	Mean	3.23	2.64
	SD	0.66	0.77
	Median	3.23	2.71
	Min.		
	Max.		

Note: LOCF = last observation carried forward.
Note: Stool consistency rated as 1 = very hard, 2 = hard, 3 = formed, 4 = loose, 5 = watery.

Source: ALOS050DEV:[S3BA3002.TABLELIB.IBSDP]DP_ITT_STOOLS.SAS/QUINTILES (US)/31MAR99/14:08

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Protocol: S3BA3002
Population: ITT (Alternating)

Table A-7.42
Lower GI Parameters: Stool Consistency
By Month: LOCF

Measurement	Statistic	Placebo (N=95)	Alosetron 1 mg BID (N=85)
Stool Consistency			
Baseline	n	95	85
	Mean	3.05	3.08
	SD	0.44	0.49
	Median	3.07	3.00
	Min.		
	Max.		
Month 1	n	95	85
	Mean	2.91	2.10
	SD	0.50	0.77
	Median	2.91	2.08
	Min.		
	Max.		
Month 2	n	95	85
	Mean	2.86	2.04
	SD	0.50	0.85
	Median	2.90	2.07
	Min.		
	Max.		
Month 3	n	95	85
	Mean	2.90	2.14
	SD	0.57	0.90
	Median	3.00	2.15
	Min.		
	Max.		

Note: LOCF = last observation carried forward.
Note: Stool consistency rated as 1 = very hard, 2 = hard, 3 = formed, 4 = loose, 5 = watery.

Source: ALOS050DEV:[S3BA3002.TABLELIB.IBSACD]ACD_ITT_STOOLS.SAS/QUINTILES (US)/01APR99/06:36

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Protocol: S3BA3002
Population: ITT (Diarrhea-Predominant)

Table D-7.43
Lower GI Parameters: Stool Consistency
Monthly Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=221)	Alosetron 1 mg BID (N=237)	p-value
Change in Stool Consistency				
Month 1	n	221	237	<0.001**
	Mean	-0.28	-1.03	
	SD	0.45	0.67	
	Median	-0.22	-0.89	
	Min.			
	Max.			
Month 2	n	221	237	<0.001**
	Mean	-0.29	-1.02	
	SD	0.50	0.71	
	Median	-0.23	-0.86	
	Min.			
	Max.			
Month 3	n	221	237	<0.001**
	Mean	-0.34	-0.99	
	SD	0.52	0.70	
	Median	-0.29	-0.80	
	Min.			
	Max.			

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: LOCF = last observation carried forward.
Note: Stool consistency rated as 1 = very hard, 2 = hard, 3 = formed, 4 = loose, 5 = watery.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOS050DEV:[S3BA3002.TABLELIB.IBSDP]DP_ITT_STOOL_CHG.SAS/QUINTILES (US)/31MAR99/14:12

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Protocol: S3BA3002
Population: ITT (Alternating)

Table A-7.43
Lower GI Parameters: Stool Consistency
Monthly Change from Baseline: LOCF

Measurement	Statistic	Placebo (N=95)	Alosetron 1 mg BID (N=85)	p-value
Change in Stool Consistency				
Month 1	n	95	85	<0.001**
	Mean	-0.14	-0.98	
	SD	0.46	0.76	
	Median	-0.14	-1.00	
	Min.			
	Max.			
Month 2	n	95	85	<0.001**
	Mean	-0.19	-1.03	
	SD	0.50	0.83	
	Median	-0.11	-0.89	
	Min.			
	Max.			
Month 3	n	95	85	<0.001**
	Mean	-0.15	-0.94	
	SD	0.62	0.86	
	Median	-0.11	-0.76	
	Min.			
	Max.			

* Significant at the 0.050 level; ** significant at the 0.010 level.
Note: LOCF = last observation carried forward.
Note: Stool consistency rated as 1 = very hard, 2 = hard, 3 = formed, 4 = loose, 5 = watery.
Note: P-value is the result of the van Elteren method of the Wilcoxon rank-sum test with stratification for cluster.

Source: ALOS050DEV:[S3BA3002.TABLELIB.IBSACD]ACD_ITT_STOOL_CHG.SAS/QUINTILES (US)/01APR99/06:36

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