Table A.10.1 Patient's Assessment of Arthritis Pain (protocol 054)

TABLE 10
PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)
BASELINE					
N	217	216	207	212	207
MEAN	68.2	68.7	67.2	67.6	67.3
STD DEV	14.87	16.52	16.99	15.69	16.67
WEEK 2					
N	217	216	207	213	207
MEAN	57.0	49.4	43.7	44.2	41.0
STD DEV	24.68	25.80	26.09	27.11	25.16
WEEK 6					
N	217	216	207	213	207
MEAN	55.6	47.8	43.0	44.9	43.7
STD DEV	26.12	28.15	27.33	29.65	27.11
WEEK 12					
N	217	216	207	213	207
MEAN	57.4	50.0	44.6	45.0	45.9
STD DEV	25.71	28.69	29.13	28.89	27.12

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with lower score as better

TABLE 10
PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-11.2	-19.3	-23.6	-23.6	-25.4	<0.001	<0.001
STD DEV	23.62	24.87	25.40	25.68	24.95		
LS MEAN CHANGE (c)	-11.8	-19.7	-24.4	-24.4	-26.5		
WEEK 6							
OBSERVED MEAN CHANGE	-12.6	-20.9	-24.2	-22.8	-23.6	<0.001	<0.001
STD DEV	25.31	27.04	26.97	28.87	27.68		
LS MEAN CHANGE (c)	-13.2	-21.5	-25.1	-23.9	-24.8		
WEEK 12							
OBSERVED MEAN CHANGE	-10.8	-18.7	-22.6	-18.8	-21.4	<0.001	<0.001
STD DEV	25.87	28.24	28.25	28.67	28.25		
LS MEAN CHANGE (c)	-11.1	-19.0	-23.3	-19.3	-22.3		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e): 50MG BID VS. NAPROXEN; 100MG BID VS. NAPROXEN; 200MG BID VS. NAPROXEN

	50MG BID VS. NAPROXEN	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN
WEEK 2:	0.74 (0.60 to 0.91)	0.94 (0.76 to 1.16)	0.92 (0.77 to 1.10)
WEEK 6:	0.87 (0.69 to 1.08)	1.01 (0.82 to 1.24)	0.96 (0.78 to 1.19)
WEEK 12:	0.85 (0.66 to 1.10)	1.05 (0.83 to 1.32)	0.87 (0.67 to 1.12)

P-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY: 100MG BID VS. PLACEBO	PRIMARY: 200MG BID VS. PLACEBO	PRIMARY: 50MG BID VS. PLACEBO	SECONDARY: 100MG BID VS. 50MG BID	SECONDARY: 200MG BID VS. 50MG BID	SECONDARY: 200MG BID VS. 100MG BID	SECONDARY: NAPROXEN VS. PLACEBO	SECONDARY: NAPROXEN VS. 50MG BID	SECONDARY: NAPROXEN VS. 100MG BID	SECONDARY: NAPROXEN VS. 200MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.039	0.036	0.980	<0.001	0.003	0.350	0.360
WEEK 6:	<0.001*	<0.001*	<0.001	0.165	0.323	0.636	<0.001	0.179	0.939	0.720
WEEK 12:	<0.001*	0.001*	0.002	0.091	0.861	0.123	<0.001	0.199	0.695	0.257

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate. The corresponding ROOT MSE are: 23.26 for week 2, 25.36 for week 6, and 26.09 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table/Figure A.10.2 Patient's Assessment of Arthritis Pain (054)

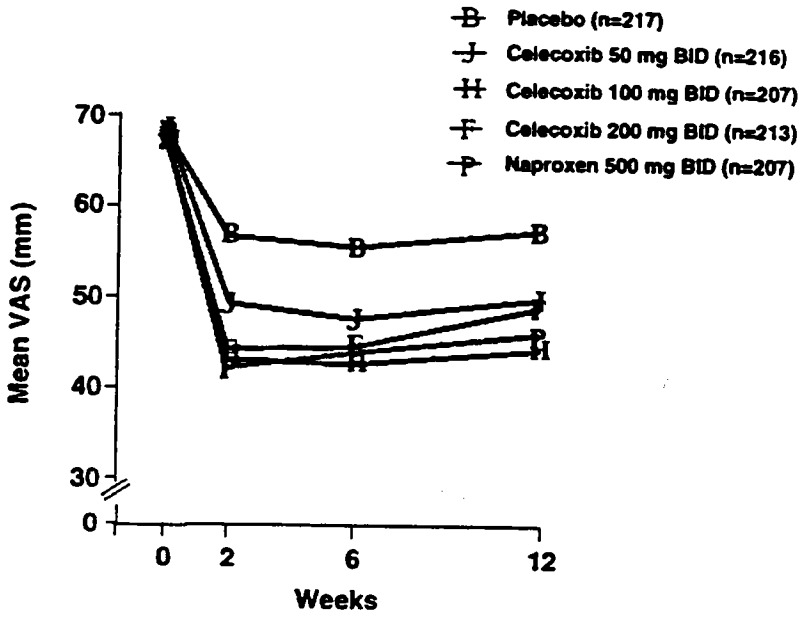


Table A.11 WOMAC pain (protocol 054)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN HIP OA
M49-96-02-056

TABLE 21.1
WOMAC PAIN
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)
BASELINE					
N	217	215	207	211	207
MEAN	10.6	10.5	10.6	10.8	10.5
STD DEV	3.25	3.40	3.33	2.95	3.54
WEEK 2					
N	217	216	207	212	207
MEAN	10.0	8.8	8.1	8.3	7.8
STD DEV	3.66	3.85	3.62	3.57	3.74
WEEK 12					
N	217	216	207	213	207
MEAN	9.7	9.0	8.5	8.5	8.0
STD DEV	3.98	3.99	4.22	4.20	3.96

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with lower score as better

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.6	-1.7	-2.5	-2.5	-2.7		
STD DEV	3.09	3.30	3.26	3.27	3.20		
LS MEAN CHANGE (c)	-0.7	-1.8	-2.6	-2.5	-2.9		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.9	-1.5	-2.1	-2.4	-2.5		
STD DEV	3.66	3.61	3.56	3.91	3.61		
LS MEAN CHANGE (c)	-1.0	-1.7	-2.2	-2.4	-2.7		

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.004	0.009	0.804	<0.001	<0.001	0.394	0.271
WEEK 12:	<0.001	<0.001	0.034	0.093	0.024	0.607	<0.001	<0.001	0.179	0.403

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.12 WOMAC pain (protocol 020)

TABLE 21.1
WOMAC PAIN
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)
BASELINE					
N	201	197	196	201	198
MEAN	10.8	10.7	10.5	10.7	11.0
STD DEV	3.41	3.18	3.36	3.36	2.97
WEEK 2					
N	201	197	196	201	198
MEAN	10.0	8.7	7.6	7.9	8.2
STD DEV	3.99	3.77	3.79	3.80	4.00
WEEK 12					
N	201	197	196	201	198
MEAN	9.4	8.6	7.4	7.9	8.4
STD DEV	4.40	4.09	4.17	4.19	4.25

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with lower score as better

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.8	-2.0	-2.9	-2.8	-2.8		
STD DEV	2.98	3.18	3.29	3.56	3.85		
LS MEAN CHANGE (c)	-0.7	-2.0	-3.0	-2.8	-2.7		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-1.4	-2.1	-3.1	-2.8	-2.6		
STD DEV	3.84	3.59	3.66	3.84	3.91		
LS MEAN CHANGE (c)	-1.2	-2.0	-3.1	-2.7	-2.4		

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.001	0.310	0.520	<0.001	0.024	0.240	0.751
WEEK 12:	<0.001	<0.001	0.026	0.002	0.969	0.259	0.001	0.320	0.038	0.339

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.13 WOMAC stiffness (protocol 054)

TABLE 21.2
WOMAC JOINT STIFFNESS
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)
BASELINE					
N	217	216	207	211	205
MEAN	4.6	4.7	4.6	4.7	4.6
STD DEV	1.42	1.48	1.54	1.60	1.60
WEEK 2					
N	217	216	207	212	207
MEAN	4.4	4.0	3.7	3.7	3.6
STD DEV	1.49	1.57	1.60	1.62	1.63
WEEK 12					
N	217	216	207	213	207
MEAN	4.3	3.9	3.7	3.7	3.6
STD DEV	1.58	1.61	1.77	1.68	1.66

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 8 with lower score as better

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.3	-0.8	-1.0	-1.0	-1.0		
STD DEV	1.37	1.45	1.59	1.56	1.54		
LS MEAN CHANGE (c)	-0.3	-0.8	-1.0	-1.0	-1.1		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.3	-0.8	-0.8	-1.0	-1.0		
STD DEV	1.61	1.50	1.67	1.75	1.56		
LS MEAN CHANGE (c)	-0.4	-0.8	-1.0	-1.0	-1.1		

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.044	0.031	0.895	<0.001	0.007	0.698	0.564
WEEK 12:	<0.001	<0.001	0.004	0.148	0.132	0.959	<0.001	0.017	0.354	0.379

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 8 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.14 WOMAC stiffness (protocol 020)

TABLE 21.2
WOMAC JOINT STIFFNESS
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)
BASELINE					
N	202	197	196	201	195
MEAN	4.9	4.8	4.7	4.9	5.0
STD DEV	1.35	1.31	1.47	1.50	1.40
WEEK 2					
N	202	197	196	201	195
MEAN	4.5	3.9	3.5	3.6	3.7
STD DEV	1.59	1.64	1.65	1.62	1.69
WEEK 12					
N	202	197	196	201	195
MEAN	4.3	3.9	3.5	3.7	3.7
STD DEV	1.72	1.73	1.71	1.69	1.81

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 8 with lower score as better

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-0.4	-0.9	-1.2	-1.3	-1.1	<0.001	<0.001
STD DEV	1.33	1.49	1.58	1.66	1.83		
LS MEAN CHANGE (c)	-0.3	-0.9	-1.2	-1.2	-1.1		
WEEK 12							
OBSERVED MEAN CHANGE	-0.6	-0.9	-1.2	-1.2	-1.2	<0.001	<0.001
STD DEV	1.61	1.60	1.57	1.71	1.90		
LS MEAN CHANGE (c)	-0.5	-0.9	-1.2	-1.1	-1.1		

P-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.019	0.027	0.874	<0.001	0.091	0.510	0.613
WEEK 12:	<0.001	<0.001	0.013	0.028	0.149	0.447	<0.001	0.154	0.446	0.995

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 8 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.15 WOMAC function (protocol 054)

TABLE 21.3
WOMAC PHYSICAL FUNCTIONING
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)
BASELINE					
N	217	215	207	211	207
MEAN	35.5	34.1	34.9	35.4	34.7
STD DEV	11.30	12.29	12.14	11.13	10.21
WEEK 2					
N	217	215	207	212	207
MEAN	33.3	29.2	27.2	27.6	26.5
STD DEV	12.60	12.73	13.32	12.71	12.43
WEEK 12					
N	217	215	207	213	207
MEAN	32.5	29.3	28.2	28.2	26.7
STD DEV	12.99	13.64	14.75	13.79	13.22

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 68 with lower score as better

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-2.2	-4.9	-7.7	-7.9	-8.2	<0.001	<0.001
STD DEV	9.28	10.36	10.11	10.72	9.96		
LS MEAN CHANGE (e)	-2.3	-5.4	-8.0	-8.1	-8.7		
WEEK 12							
OBSERVED MEAN CHANGE	-3.0	-4.8	-6.7	-7.1	-7.9	<0.001	<0.001
STD DEV	10.94	10.91	11.37	12.28	11.34		
LS MEAN CHANGE (e)	-3.2	-5.5	-7.0	-7.5	-8.4		

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.005	0.006	0.965	<0.001	<0.001	0.470	0.511
WEEK 12:	<0.001	<0.001	0.023	0.142	0.047	0.609	<0.001	0.004	0.160	0.369

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 68 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.16 WOMAC function (protocol 020)

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)
BASELINE					
N	184	174	176	181	180
MEAN	36.0	36.2	35.4	35.3	36.0
STD DEV	10.83	10.76	11.77	12.29	10.56
WEEK 2					
N	184	174	176	181	180
MEAN	33.0	29.3	26.2	26.9	28.1
STD DEV	12.52	11.06	12.88	12.94	13.23
WEEK 12					
N	184	174	176	181	180
MEAN	31.7	29.4	26.1	27.4	28.5
STD DEV	13.94	14.09	14.38	14.20	14.92

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 68 with lower score as better

TABLE 21.3
WOMAC PHYSICAL FUNCTIONING
PART 2 OF 2: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-2.9	-6.9	-9.1	-8.4	-8.5		
STD DEV	9.32	9.85	11.19	11.39	12.53		
LS MEAN CHANGE (c)	-2.6	-6.8	-9.3	-8.5	-8.0		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-6.3	-6.8	-9.2	-7.9	-8.1		
STD DEV	11.21	11.61	12.26	12.62	13.13		
LS MEAN CHANGE (c)	-5.9	-6.8	-9.5	-8.1	-7.8		

P-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.021	0.113	0.460	<0.001	0.257	0.233	0.647
WEEK 12:	<0.001	<0.001	0.018	0.033	0.301	0.265	0.001	0.438	0.170	0.794

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 68 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.17 WOMAC composite (protocol 054)

TABLE 21.4
WOMAC COMPOSITE SCORE
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)
BASELINE					
N	217	214	207	211	205
MEAN	50.7	49.3	50.2	50.9	49.8
STD DEV	14.98	16.27	16.06	14.33	16.55
WEEK 2					
N	217	215	207	212	207
MEAN	47.7	46.0	39.0	39.6	37.9
STD DEV	16.85	17.40	17.80	17.09	16.96
WEEK 12					
N	217	215	207	213	207
MEAN	46.5	42.2	40.4	40.3	38.4
STD DEV	17.66	18.66	19.99	18.92	17.97

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 96 with lower score as better

WOMAC COMPOSITE SCORE
PART 2 OF 2: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-3.1	-7.3	-11.2	-11.4	-12.0		
STD DEV	12.59	13.97	13.91	14.22	13.74		
LS MEAN CHANGE (c)	-3.4	-8.0	-11.7	-11.7	-12.7		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-4.2	-7.2	-9.7	-10.6	-11.5		
STD DEV	15.07	14.73	15.28	16.83	15.45		
LS MEAN CHANGE (c)	-4.6	-8.0	-10.3	-11.0	-12.4		

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.003	0.002	0.965	<0.001	<0.001	0.393	0.402
WEEK 12:	<0.001	<0.001	0.014	0.217	0.034	0.613	<0.001	0.002	0.138	0.329

(a) This table is based on the last observation carried forward approach.
(b) Scale ranged from 0 to 96 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.18 WOMAC composite (protocol 020)

TABLE 21.4
WOMAC COMPOSITE SCORE
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)
BASELINE					
N	182	174	175	181	177
MEAN	51.6	51.8	50.5	51.0	52.9
STD DEV	14.80	14.39	15.67	16.36	13.97
WEEK 2					
N	182	174	175	181	177
MEAN	47.5	42.1	37.4	36.5	40.3
STD DEV	17.34	17.66	17.46	17.69	18.50
WEEK 12					
N	182	174	175	181	177
MEAN	45.5	42.3	37.2	39.0	41.0
STD DEV	19.32	19.25	19.46	19.31	20.69

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 96 with lower score as better

TABLE 21.4
WOMAC COMPOSITE SCORE
PART 2 OF 2: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT) - KNEE PATIENTS ONLY

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=198)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-4.1	-9.7	-13.1	-12.5	-12.7	<0.001	<0.001
STD DEV	12.55	13.52	14.91	15.76	17.19		
LS MEAN CHANGE (c)	-3.6	-9.7	-13.4	-12.5	-11.9		
WEEK 12							
OBSERVED MEAN CHANGE	-6.1	-9.5	-13.3	-12.0	-11.9	<0.001	<0.001
STD DEV	15.58	15.76	16.40	17.45	18.19		
LS MEAN CHANGE (c)	-5.6	-9.6	-13.6	-12.1	-11.3		

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS PLACEBO	200MG BID VS. PLACEBO	50MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.012	0.052	0.549	<0.001	0.137	0.296	0.650
WEEK 12:	<0.001	<0.001	0.016	0.039	0.146	0.354	<0.001	0.325	0.173	0.655

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 96 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c). Naproxen group was excluded
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.19 Withdrawal due to lack of Arthritis Efficacy (020, 054)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN OA
M49-96-02-020

TABLE 22
INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=203)	SC-58635 50MG BID (N=203)	SC-58635 100MG BID (N=197)	SC-58635 200MG BID (N=202)	NAPROXEN 500MG BID (N=196)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	79(39%)	61(30%)	40(20%)	49(24%)	53(26%)

p-VALUES FOR OVERALL COMPARISONS (a): <0.001

p-VALUE FOR LINEAR TREND TEST (b): <0.001

p-VALUES FOR TREATMENT COMPARISONS (c):

50MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
0.076	<0.001	0.002	0.029	0.219	0.400	0.008	0.438	0.190	0.647

(a) Fisher's Exact test for all five treatment groups
(b) Cochran-Mantel-Haenszel test of linear dose trend (Nonzero Correlation), Naproxen group was excluded
(c) Pairwise Fisher's Exact test

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN HIP OA
M49-96-02-054

TABLE 22
INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=217)	SC-58635 50MG BID (N=216)	SC-58635 100MG BID (N=207)	SC-58635 200MG BID (N=213)	NAPROXEN 500MG BID (N=207)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	113(52%)	76(35%)	61(29%)	55(26%)	51(25%)

p-VALUES FOR OVERALL COMPARISONS (a): <0.001

p-VALUE FOR LINEAR TREND TEST (b): <0.001

p-VALUES FOR TREATMENT COMPARISONS (c):

50MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
<0.001	<0.001	<0.001	0.214	0.037	0.445	<0.001	0.020	0.319	0.823

(a) Fisher's Exact test for all five treatment groups
(b) Cochran-Mantel-Haenszel test of linear dose trend (Nonzero Correlation), Naproxen group was excluded
(c) Pairwise Fisher's Exact test

Table A.20 Time to Withdrawal-Lack of Arthritis Efficacy (054)

TABLE 22
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 1 OF 2: KAPLAN-MEIER ESTIMATES OF PROPORTION OF PATIENTS
WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY
INTENT-TO-TREAT COHORT (ITT)

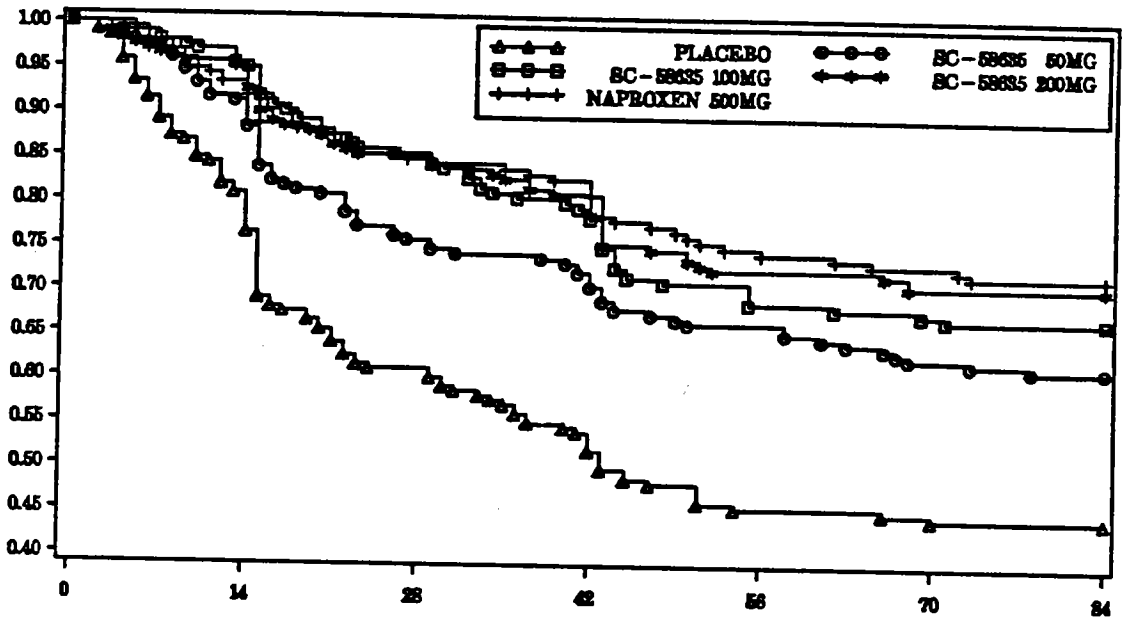


TABLE 23
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 2 OF 2: LOG-RANK TESTS FOR TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

p-VALUE FOR OVERALL COMPARISONS (a): <0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

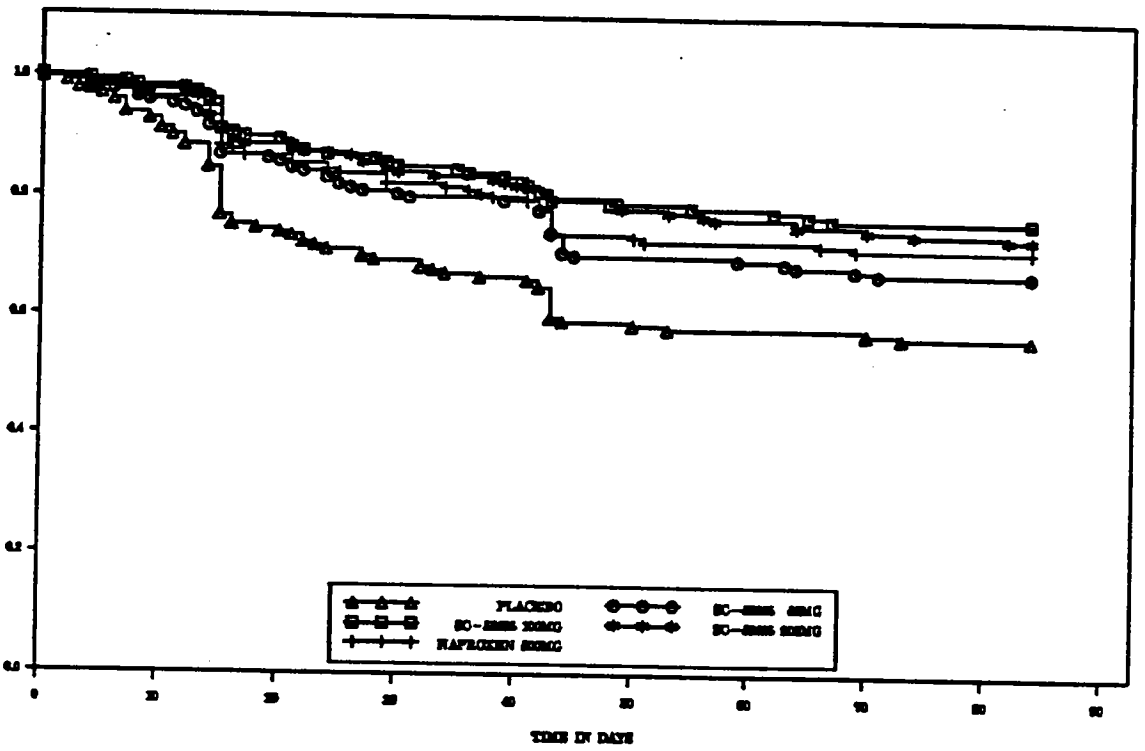
50MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
<0.001	<0.001	<0.001	0.159	0.046	0.544	<0.001	0.026	0.369	0.772

(a) From log-rank test for all five treatment groups
(b) From pairwise log-rank test

Table A.21 Time to Withdrawal-Lack of Arthritis Efficacy (020)

TABLE 22
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 1 OF 2: KAPLAN-MEIER ESTIMATES OF PROPORTION OF PATIENTS WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)



TIME IN DAYS

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN OA
2M9-96-02-020

TABLE 23
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 2 OF 2: LOG-RANK TESTS FOR TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

p-VALUE FOR OVERALL COMPARISONS (a): <0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

50MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	100MG BID VS. 50MG BID	200MG BID VS. 50MG BID	200MG BID VS. 100MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 50MG BID	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID
0.017	<0.001	<0.001	0.061	0.163	0.648	0.002	0.420	0.295	0.530

(a) From log-rank test for all five treatment groups
(b) From pairwise log-rank test

Table A.22.1 Reasons for Study Termination (020, 021, 054)

Study	Number of Osteoarthritis Patients by Treatment Group				
		Celecoxib			Naproxen
	Placebo	50 mg BID	100 mg BID	200 mg BID	500 mg BID
Study 020[a]	(n=204[b])	(n=203)	(n=197)	(n=202)	(n=198)
Total Completed	91 (45%)	118 (58%)	116 (59%)	129 (64%)	116 (59%)
Total Withdrawn	113[b] (55%)	85 (42%)	81 (41%)	73 (36%)	82 (41%)
Lost to Follow-up	3 (1%)	1 (<1%)	3 (2%)	1 (<1%)	3 (2%)
Pre-Existing Violation	3 (1%)	1 (<1%)	0 (0%)	0 (0%)	1 (<1%)
Protocol Non-Compliance	12 (6%)	4 (2%)	7 (4%)	2 (<1%)	8 (4%)
Treatment Failure	79 (39%)	61 (30%)	40 (20%)	49 (24%)	52 (26%)
Adverse Event	16 (8%)	18 (9%)	31 (16%)	21 (10%)	18 (9%)
Study 021[a]	(n=242)	(n=252)	(n=240[b])	(n=233)	(n=226)
Total Completed	119 (49%)	168 (67%)	165 (69%)	154 (66%)	147 (65%)
Total Withdrawn	123 (51%)	84 (33%)	75[b] (31%)	79 (34%)	79 (35%)
Lost to Follow-up	5 (2%)	1 (<1%)	0 (0%)	2 (<1%)	1 (<1%)
Pre-Existing Violation	2 (<1%)	3 (1%)	1 (<1%)	1 (<1%)	0 (0%)
Protocol Non-Compliance	13 (5%)	8 (3%)	7 (3%)	4 (2%)	8 (4%)
Treatment Failure	89 (37%)	56 (22%)	51 (21%)	49 (21%)	40 (18%)
Adverse Event	14 (6%)	16 (6%)	16 (7%)	23 (10%)	30 (13%)
Study 054	(n=218[b])	(n=216)	(n=207)	(n=213)	(n=207)
Total Completed	79 (36%)	111 (51%)	111 (54%)	119 (56%)	118 (57%)
Total Withdrawn	139[b] (64%)	105 (49%)	96 (46%)	94 (44%)	89 (43%)
Lost to Follow-up	2 (<1%)	4 (2%)	0 (0%)	2 (<1%)	1 (<1%)
Pre-Existing Violation	3 (1%)	2 (<1%)	0 (0%)	3 (1%)	1 (<1%)
Protocol Non-Compliance	5 (2%)	6 (3%)	8 (4%)	9 (4%)	7 (3%)
Treatment Failure	112 (52%)	76 (35%)	61 (29%)	55 (26%)	51 (25%)
Adverse Event	16 (7%)	17 (8%)	27 (13%)	25 (12%)	29 (14%)
Pooled 12-Week Pivotal Studies	(n=664[b])	(n=671)	(n=644[b])	(n=648)	(n=631)
Total Completed	289 (44%)	397 (59%)	392 (61%)	402 (62%)	381 (60%)
Total Withdrawn	375[b] (56%)	274 (41%)	252[b] (39%)	246 (38%)	250 (40%)
Lost to Follow-up	10 (2%)	6 (2%)	3 (<1%)	5 (<1%)	5 (<1%)
Pre-Existing Violation	8 (1%)	6 (2%)	1 (<1%)	4 (<1%)	2 (<1%)
Protocol Non-Compliance	30 (4%)	18 (6%)	22 (3%)	15 (2%)	23 (4%)
Treatment Failure	284 (42%)	193 (29%)	152 (24%)	153 (24%)	143 (23%)
Adverse Event	46 (7%)	51 (8%)	74 (11%)	69 (11%)	77 (12%)

Derived from Individual Study Reports

a) Includes only patients with OA of the knee.

b) Total number of patients includes three patients (one in the placebo group [Study 020], one in the placebo group [Study 054], and one in the celecoxib 100 mg BID group [Study 021]), who were randomized into a study but did not receive study medication and are not included in the ITT Cohort.

Table A.22.2 Reasons for Study Termination (060, 087)

Study	Number of Osteoarthritis Patients by Treatment Group		
		Celecoxib	
	Placebo	100 mg BID	200 mg QD
Study 060	(n=232)	(n=231)	(n=223)
Total Completed	146 (63%)	194 (84%)	182 (82%)
Total Withdrawn	86 (37%)	37 (16%)	41 (18%)
Lost to Follow-up	2 (<1%)	4 (2%)	2 (<1%)
Pre-Existing Violation	2 (<1%)	2 (<1%)	2 (<1%)
Protocol Non-Compliance	6 (3%)	2 (<1%)	7 (3%)
Treatment Failure	56 (24%)	18 (8%)	21 (9%)
Adverse Event	20 (9%)	11 (5%)	9 (4%)
Study 087	(n=244)	(n=243)	(n=231)
Total Completed	164 (67%)	194 (80%)	191 (83%)
Total Withdrawn	80 (33%)	49 (20%)	40 (17%)
Lost to Follow-up	1 (<1%)	0 (0%)	1 (<1%)
Pre-Existing Violation	4 (2%)	6 (2%)	4 (2%)
Protocol Non-Compliance	8 (3%)	7 (3%)	5 (2%)
Treatment Failure	55 (23%)	27 (11%)	24 (10%)
Adverse Event	12 (5%)	9 (4%)	6 (3%)
Pooled 6-Week Pivotal Studies	(n=476)	(n=474)	(n=454)
Total Completed	310 (65%)	388 (82%)	373 (82%)
Total Withdrawn	166 (35%)	86 (18%)	81 (18%)
Lost to Follow-up	3 (1%)	4 (1%)	3 (1%)
Pre-Existing Violation	6 (1%)	8 (2%)	6 (1%)
Protocol Non-Compliance	14 (3%)	9 (2%)	12 (3%)
Treatment Failure	111 (23%)	45 (9%)	45 (10%)
Adverse Event	32 (7%)	20 (4%)	15 (3%)

Derived from Individual Study Reports

Table A.23 Schedule of Observations and Procedures (Protocol 060)

	Pretreatment Period		Treatment Period		
	Screening Visit (-14 to-2 days)	Baseline Visit (Day 0)	Week 2 (Day 14) (±2 days)	Week 6 (Day 42) (±4 days)	Early Termination
Informed Consent	x				
Medical History	x				
Physical Exam	x			x	x
Clinical Lab Tests[a]	x		x	x	x
SF-36 Health Survey		x		x	x
OA Assessments[b]	x[c]	x	x	x	x
Discontinued NSAID or Analgesic[d]	x				
Meet Flare Criteria		x			
Signs & Symptoms		x	x	x	x
Dispense Study Med		x	x		
Return & Count Study Med			x	x	x
Dispense Con Med Diary Card		x	x		
Retrieve Con Med Diary Card			x	x	x
Blood Sample For PK[e]			x	x	

(a) Clinical laboratory tests included: **Hematology** (white blood cell [WBC] count, hemoglobin, hematocrit, platelet count [estimate not acceptable]) and **Biochemistry** (BUN, creatinine, total bilirubin, alkaline phosphatase, AST [SGOT], ALT [SGPT], creatine kinase [CK]). **Urinalysis** (pH, specific gravity, WBC, red blood cell [RBC], protein, glucose, ketones, bilirubin) at Screening Visit only. Serum pregnancy test for women of childbearing potential at Screening Visit only.

(b) Patient's Global Assessment of Arthritic Condition, Patient's Assessment of Pain - Visual Analog Scale (VAS), Physician's Global Assessment of Arthritic Condition, Functional Capacity Classification, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Osteoarthritis Severity Index.

(c) Screening arthritis assessment data was not collected by Searle. Patient's Assessment of Pain (VAS) and WOMAC were not performed at the Screening Visit.

(d) Patient discontinued NSAID or analgesic use within 48 hours or at least five half-lives before the Baseline Arthritis Assessments, whichever was greater.

(e) Blood samples were collected at selected investigational sites only.

Table A.24.1 Patient's global assessment (protocol 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
969-98-02-087

TABLE 15
PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT TO TREAT COHORT (ITT) *

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)
BASELINE			
N	243	241	231
MEAN	3.9	3.8	3.8
STD DEV	0.65	0.58	0.65
WEEK 2			
N	243	241	231
MEAN	3.6	2.7	2.7
STD DEV	0.92	0.90	0.85
WEEK 6			
N	243	241	231
MEAN	3.0	2.8	2.6
STD DEV	1.00	0.99	0.95

(a) This table is based on the last observation carried forward approach
(b) Scale ranges from 1 (very good) to 5 (very poor)
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)	P VALUE (d)
WEEK 2				
IMPROVED (b)	76(31%)	94(41%)	71(31%)	<0.001
NO CHANGE	176(72%)	137(57%)	160(69%)	
WORSENED (c)	11(5%)	5(2%)	0(0%)	
TOTAL	243(100%)	241(100%)	231(100%)	
WEEK 6				
IMPROVED (b)	65(27%)	90(37%)	67(29%)	0.006
NO CHANGE	163(66%)	143(59%)	163(71%)	
WORSENED (c)	18(7%)	8(3%)	1(<1%)	
TOTAL	243(100%)	241(100%)	231(100%)	

P VALUES FOR TREATMENT COMPARISONS (d) :

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 2:	<0.001	0.009	0.107
WEEK 6:	0.020	0.001	0.479

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from Baseline for grades 3-5 or a change in grade from 2 to 1
(c) Worsened is defined as an increase of at least two grades from Baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Haenszel test stratified by center (Row Mean Scores Differ)

Table A.24.2 Patient's Global Assessment (Protocol 087)

SC-58635 QD VS BID EFFICACY IN RHEU OA
X49 94-02 087

TABLE 15
PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 3 OF 4: MEAN CHANGE ANALYSIS (a) (b)

INTENT TO-TREAT COHORT (ITT)

	PLACEBO (N=243)	SC-58635 100MG BID (N=241)	SC-58635 200MG QD (N=231)	p-VALUE(c)
WEEK 2				
OBSERVED MEAN CHANGE	-0.8	-1.2	-1.1	<0.001
STD DEV	0.99	0.99	0.94	
LS MEAN CHANGE (c)	-0.8	-1.1	-1.1	
WEEK 6				
OBSERVED MEAN CHANGE	-0.8	-1.1	-1.2	<0.001
STD DEV	1.10	1.06	1.05	
LS MEAN CHANGE (c)	-0.8	1.1	-1.2	

Q-RATIO WITH 95% CONFIDENCE INTERVALS (d): 200MG QD VS. 100MG BID

WEEK 2:	1.00 (0.84 to 1.15)
WEEK 6:	1.13 (0.94 to 1.33)

P-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 2:	<0.001	<0.001	0.963
WEEK 6:	0.006	<0.001	0.136

(a) This table is based on the last observation carried forward approach
(b) Scale ranges from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 0.847 for week 2, and 0.973 for week 6
(d) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 200MG QD versus SC-58635 100MG BID
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.25.1 Physician's Global Assessment (protocol 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
#49-98-02-087

TABLE 17
PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)
BASELINE			
N	243	240	231
MEAN	3.8	3.8	3.7
STD DEV	0.57	0.61	0.59
WEEK 2			
N	241	241	231
MEAN	3.0	2.6	2.7
STD DEV	0.83	0.84	0.79
WEEK 6			
N	243	241	231
MEAN	3.0	2.7	2.6
STD DEV	0.85	0.91	0.89

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor)

	PLACEBO (N=243)	SC-58635 100MG BID (N=241)	SC-58635 200MG QD (N 231)	p-VALUE (d)
WEEK 2				<0.001
IMPROVED (b)	47(19%)	93(39%)	66(29%)	
NO CHANGE	188(77%)	144(60%)	164(71%)	
WORSENED (c)	8(3%)	3(1%)	1(<1%)	
TOTAL	243(100%)	240(100%)	231(100%)	
WEEK 6				0.011
IMPROVED (b)	59(24%)	84(35%)	80(35%)	
NO CHANGE	172(71%)	151(63%)	151(65%)	
WORSENED (c)	12(5%)	6(2%)	0(0%)	
TOTAL	243(100%)	240(100%)	231(100%)	

P VALUES FOR TREATMENT COMPARISONS (d):

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 2:	<0.001	0.008	0.022
WEEK 6:	0.022	0.006	0.833

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1
(c) Worsened is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Haenszel test stratified by center (Row Mean Scores Differ)

Table A.25.2 Physician's Global Assessment (protocol 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
M49-98-02-087

TABLE 17
PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 3 OF 4: MEAN CHANGE ANALYSIS (a) (b)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N=263)	SC-58635 100MG BID (N=241)	SC-58635 200MG QD (N=231)	P VALUES(c)
WEEK 2				
OBSERVED MEAN CHANGE	-0.8	-1.2	-1.1	<0.001
STD DEV	0.90	0.87	0.84	
LS MEAN CHANGE (c)	-0.7	-1.1	-1.1	
WEEK 6				
OBSERVED MEAN CHANGE	-0.8	-1.1	-1.2	<0.001
STD DEV	1.01	0.96	1.01	
LS MEAN CHANGE (c)	-0.8	-1.0	-1.2	

O-RATIO WITH 95% CONFIDENCE INTERVALS (d): 200MG QD VS. 100MG BID

WEEK 2:	0.96 (0.84 to 1.10)
WEEK 6:	1.13 (0.97 to 1.32)

P-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 2:	<0.001	<0.001	0.553
WEEK 6:	0.003	<0.001	0.126

a: This table is based on the last observation carried forward approach.
b: The change from baseline every week to every week with negative change indicating improvement
c: From Analysis of Covariance model with treatment and center as factors and baseline value as covariate.
The corresponding MSE MSE are: 0.796 for week 2, and 0.890 for week 6
d: O-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 200MG QD versus SC-58635 100MG BID
e: From a contrast statement from Analysis of Covariance model in (c)

Table A.26 Patient's Assessment of Arthritis Pain (protocol 060)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=231)	SC-58635 200MG QD (N=222)
BASELINE			
N	231	231	222
MEAN	68.1	67.8	68.0
STD DEV	15.16	16.52	16.74
WEEK 2			
N	231	231	222
MEAN	55.5	42.7	43.0
STD DEV	24.65	24.59	23.75
WEEK 6			
N	231	231	222
MEAN	54.0	40.3	41.0
STD DEV	26.00	28.01	26.29

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with lower score as better

SC-58635 QD VS BID EFFICACY IN KNEE OA
B49-96-02-060

TABLE 17
PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=231)	SC-58635 200MG QD (N=222)	P-VALUE(c)
WEEK 2				
OBSERVED MEAN CHANGE	-12.6	-25.1	-25.9	<0.001
STD DEV	24.55	25.38	25.05	
LS MEAN CHANGE (c)	-13.9	-25.5	-26.1	
WEEK 6				
OBSERVED MEAN CHANGE	-14.1	-27.5	-26.9	<0.001
STD DEV	25.88	27.78	28.41	
LS MEAN CHANGE (c)	-14.6	-28.5	-27.7	

Q-RATIO WITH 95% CONFIDENCE INTERVALS (d): 200MG QD VS. 100MG BID

WEEK 2:	1.02 (0.85 to 1.22)
WEEK 6:	0.97 (0.81 to 1.17)

p-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 2:	<0.001	<0.001	0.788
WEEK 6:	<0.001	<0.001	0.747

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 23.37 for week 2, and 25.69 for week 6
(d) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 200MG QD versus SC-58635 100MG BID
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.27 Patient's Assessment of Arthritis Pain (protocol 087)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)
BASELINE			
N	243	241	231
MEAN	68.2	67.6	65.2
STD DEV	16.51	16.47	16.42
WEEK 2			
N	243	241	231
MEAN	54.1	43.5	44.4
STD DEV	25.33	26.15	23.96
WEEK 6			
N	243	241	231
MEAN	52.3	45.6	42.8
STD DEV	27.05	27.61	26.51

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with lower score as better

SC-58635 QD VS BID EFFICACY IN KNEE OA
M49 96 02-087

TABLE 16
PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)	P VALUE(c)
WEEK 2				
OBSERVED MEAN CHANGE	-14.1	-24.1	-20.8	<0.001
STD DEV	26.75	24.35	24.44	
LS MEAN CHANGE (c)	-12.4	-22.5	-21.1	
WEEK 6				
OBSERVED MEAN CHANGE	-16.0	-22.0	-22.5	0.082
STD DEV	27.39	26.92	28.74	
LS MEAN CHANGE (c)	-15.0	-21.2	-23.5	

Q-RATIO WITH 95% CONFIDENCE INTERVALS (d): 200MG QD VS. 100MG BID

WEEK 2:	0.94 (0.76 to 1.15)
WEEK 6:	1.11 (0.88 to 1.40)

P-VALUES FOR TREATMENT COMPARISONS (e):

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 2:	<0.001	<0.001	0.520
WEEK 6:	0.011	<0.001	0.344

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate.
The corresponding RMSE are: 23.82 for week 2, and 24.41 for week 6
(d) Q-RATIO is defined as the ratio of least square mean change from (c), of SC-58635 200MG QD versus SC-58635 100MG BID
(e) From a contrast statement from Analysis of Covariance model in (c)

Table A.28 WOMAC pain (protocol 060)

SC-58635 QD VS BID EFFICACY IN KNEE OA
M69-96-02-060

TABLE 20.1
WOMAC PAIN
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=231)	SC-58635 200MG QD (N=222)
BASELINE			
N	231	230	220
MEAN	10.2	10.3	10.2
STD DEV	3.45	3.49	3.68
WEEK 6			
N	231	230	220
MEAN	8.6	7.3	7.5
STD DEV	4.80	3.89	4.19

(a) This table is based on the last observation carried forward approach.
(b) Scale ranged from 0 (= 20 with lower score as better)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=231)	SC-58635 200MG QD (N=222)	P-VALUE (c)
WEEK 6				
OBSERVED MEAN CHANGE	-1.4	-3.0	-2.7	<0.001
STD DEV	3.52	3.52	3.93	
LS MEAN CHANGE (c)	1.5	-3.1	-2.8	

P-VALUES FOR TREATMENT COMPARISONS (d):

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 6:	<0.001	<0.001	0.473

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c)

Table A.29 WOMAC pain (protocol 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
M69-98 02 087

TABLE 19.1
WOMAC PAIN
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)
BASELINE			
N	239	239	226
MEAN	10.5	10.1	10.2
STD DEV	3.33	3.33	3.52
WEEK 6			
N	242	240	231
MEAN	8.7	7.4	7.1
STD DEV	4.21	4.47	4.08

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with lower score as better

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 243)	SC-58635 100MG BID (N 241)	SC-58635 200MG QD (N 231)	P VALUE (C)
WEEK 6				
OBSERVED MEAN CHANGE	1.8	2.6	3.0	<0.001
STD DEV	4.07	4.32	4.57	
LS MEAN CHANGE (C)	-1.6	-2.6	-3.0	

P-VALUES FOR TREATMENT COMPARISONS (D)

	100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
WEEK 6:	0.005	<0.001	0.276

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 20 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate
(d) From a contrast statement from Analysis of Covariance model in (c)

Table A.30 Withdrawal due to lack of Arthritis Efficacy (060, 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
N49-96-02-060

TABLE 21
INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=231)	SC-58635 200MG QD (N=222)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	56(24%)	18(8%)	21(9%)

P-VALUES FOR OVERALL COMPARISONS (a): <0.001

P-VALUES FOR TREATMENT COMPARISONS (b):

100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
<0.001	<0.001	0.616

(a) Fisher's Exact test
(b) Pairwise Fisher's Exact test

SC-58635 QD VS BID EFFICACY IN KNEE OA
N49-96-02-087

TABLE 20
INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=243)	SC-58635 100MG BID (N=241)	SC-58635 200MG QD (N=251)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	55(23%)	27(11%)	24(10%)

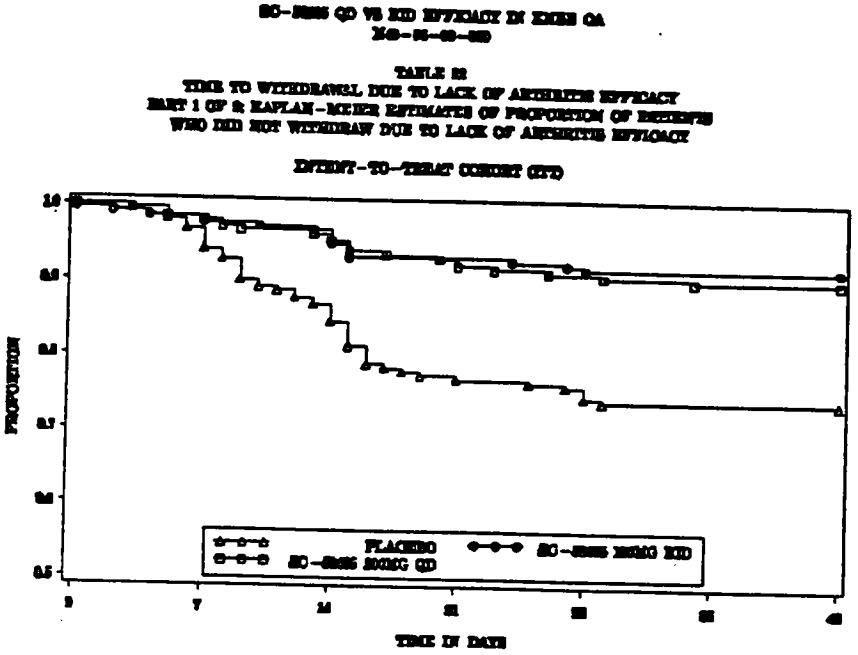
P-VALUES FOR OVERALL COMPARISONS (a): <0.001

P-VALUES FOR TREATMENT COMPARISONS (b):

100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
<0.001	<0.001	0.662

(a) Fisher's Exact test
(b) Pairwise Fisher's Exact test

Table A.31 Time to Withdrawal-Lack of Arthritis Efficacy (060, 087)



SC-58635 QD VS BID EFFICACY IN KNEE OA
M49-96-02-087

TABLE 31
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 1 OF 2: KAPLAN-MEIER ESTIMATES OF PROPORTION OF PATIENTS
WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

Table A.32 Schedule of Observations and Procedures (protocol 022)

	Screening Visit -7 to -2 day	Baseline Visit (Day 0)	Week 2 (Day 14) (_1 day)	Week 6 (Day 42) (_3 days)	Week 12 (Day 84) (_5 days)	Early Termination
Informed Consent	X					
Medical History	X					
Physical Examination	X				X	X
Clinical laboratory tests (a)	X		X	X (b)	X	X
Discontinue NSAID (c)	X					
Meet Flare Criteria		X				
C-Reactive Protein		X	X	X	X	X
Rheumatoid Factor	X					
SF-36 Health Survey		X			X	X
Health Assessment Questionnaire (HAQ)		X	X	X	X	X
RA Assessments	X (d)	X	X	X	X	X
UGI Endoscopy	X (e)				X	X
Signs and Symptoms		X	X	X	X	X
Dispense Study Medication		X	X	X		
Return and Count Study Medication			X	X	X	X
Dispense Concurrent Meds Diary Card		X	X	X		
Collect Concurrent Meds Diary Card			X	X	X	X

(a) Clinical laboratory tests included **Hematology** (white blood cell [WBC] count with differential, red blood cell [RBC] count, hemoglobin, hematocrit, platelet count [estimate not acceptable], prothrombin time [PT], and partial thromboplastin time [PTT]); **Biochemistry** (sodium, potassium, chloride, calcium, inorganic phosphorus, blood urea nitrogen [BUN], creatinine, total protein, albumin, total bilirubin, uric acid, glucose, alkaline phosphatase, AST [SGOT], ALT [SGPT], creatine kinase [CK]); and **Urinalysis** (pH, specific gravity, WBC, RBC, protein, glucose, ketones, bilirubin). FlexSure® (Baseline) and CLOtest at Final Visit for *H. pylori*. Serum pregnancy test was performed within seven days before Baseline Arthritis Assessments for women of childbearing potential.

(b) PT and PTT were not performed at the Week 6 Visit.

(c) Patients discontinued oxaprozin and/or piroxicam at least four days before the Baseline Arthritic Assessments.

(d) Screening arthritis assessment data were collected by Searle but not entered into the database.

(e) Pretreatment (Baseline) endoscopy must have been performed within seven days before the first dose of study medication.

Table A.33 Baseline demographics (study 022, 023-pooled)

Text Table 44. Pooled Baseline Demographic Characteristics and Disease Status for RA Patients By Treatment Group (All Randomized Patients: Pooled Pivotal Studies 022 and 023)

Baseline Characteristic	Number of Patients by Treatment Group				
	Placebo (n=452)	Celecoxib 100 mg BID (n=468)	Celecoxib 200 mg BID (n=454 a)	Celecoxib 400 mg BID (n=435 a)	Naproxen 500 mg BID (n=443)
Age (years)					
Mean (Std. Dev.)	54.2 (12.42)	55.1 (11.99)	54.0 (12.09)	54.0 (12.10)	55.9 (12.09)
Range	23-84	22-85	20-90	21-85	21-82
<65 years - N (%)	350 (77%)	364 (78%)	351 (77%)	344 (79%)	321 (72%)
≥65 years - N (%)	102 (23%)	104 (22%)	103 (23%)	91 (21%)	122 (28%)
Race/Ethnic Origin					
Asian - N (%)	1 (<1%)	4 (<1%)	6 (1%)	4 (<1%)	1 (<1%)
Black - N (%)	36 (8%)	42 (9%)	35 (8%)	35 (8%)	34 (8%)
Caucasian - N (%)	391 (87%)	394 (84%)	380 (84%)	364 (84%)	377 (85%)
Hispanic - N (%)	23 (5%)	25 (5%)	32 (7%)	28 (6%)	28 (6%)
Other - N (%)	1 (<1%)	3 (<1%)	1 (<1%)	4 (<1%)	3 (<1%)
Gender					
Female - N (%)	336 (74%)	346 (74%)	328 (72%)	314 (72%)	313 (71%)
Male - N (%)	116 (26%)	122 (26%)	126 (28%)	121 (28%)	130 (29%)
Disease Duration - Years					
Mean (Std. Dev.)	10.3 (±9.91)	10.7 (±9.01)	10.4 (±9.32)	10.3 (±8.77)	11.0 (±9.80)
Range					
<5 years - N (%)	159 (35%)	135 (29%)	166 (37%)	150 (34%)	143 (32%)
≥5 years - N (%)	293 (65%)	333 (71%)	288 (63%)	285 (66%)	300 (68%)
Corticosteroid Use					
Yes - N (%)	175 (39%)	209 (45%)	172 (38%)	154 (35%)	167 (38%)
No - N (%)	277 (61%)	259 (55%)	282 (62%)	281 (65%)	276 (62%)
Methotrexate Use					
Yes - N (%)	192 (42%)	221 (47%)	205 (45%)	202 (46%)	200 (45%)
No - N (%)	260 (58%)	247 (53%)	249 (55%)	233 (54%)	243 (55%)
Other DMARD Use					
Yes - N (%)	148 (33%)	153 (33%)	139 (31%)	132 (30%)	149 (34%)
No - N (%)	304 (67%)	315 (67%)	315 (69%)	303 (70%)	294 (66%)

Pooled Pivotal Studies 022 and 023)

Baseline Measure	Number of Patients by Treatment Group				
	Placebo (n=452)	Celecoxib 100 mg BID (n=468)	Celecoxib 200 mg BID (n=454 a)	Celecoxib 400 mg BID (n=435 a)	Naproxen 500 mg BID (n=443)
Patient's Global Assessment of Arthritic Condition - N (%)					
Very Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fair	169 (37%)	181 (39%)	184 (41%)	175 (40%)	189 (43%)
Poor	227 (50%)	230 (49%)	212 (47%)	204 (47%)	209 (47%)
Very Poor	56 (12%)	57 (12%)	58 (13%)	56 (13%)	45 (10%)
Number of Tender/Painful Joints					
Mean (Std. Dev.)	28.7 (14.55)	28.2 (14.40)	29.6 (14.99)	28.8 (14.36)	28.2 (14.01)
Range					
Number of Swollen Joints					
Mean (Std. Dev.)	20.9 (11.83)	20.5 (11.68)	21.7 (12.29)	20.7 (11.80)	20.6 (12.11)
Range					
Physician's Global Assessment of Arthritic Condition - N (%)					
Very Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Good	0 (0%)	1 (<1%)	0 (0%)	0 (0%)	0 (0%)
Fair	199 (44%)	207 (44%)	183 (40%)	182 (42%)	191 (43%)
Poor	220 (49%)	218 (47%)	227 (50%)	216 (50%)	219 (50%)
Very Poor	33 (7%)	42 (9%)	44 (10%)	37 (9%)	32 (7%)

Table A.34.1 Physician's Global Assessment (Protocol 023)

TABLE 20
PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	221	228	218	217	218
MEAN	3.6	3.7	3.7	3.7	3.7
STD DEV	0.61	0.65	0.64	0.62	0.63
WEEK 2					
N	221	228	218	217	218
MEAN	3.3	2.8	2.7	2.8	2.7
STD DEV	0.90	0.86	0.84	0.80	0.82
WEEK 6					
N	221	228	218	217	218
MEAN	3.2	2.9	2.8	2.8	2.7
STD DEV	1.01	0.93	0.95	0.91	0.87
WEEK 12					
N	221	228	218	217	218
MEAN	3.3	3.0	2.9	2.8	2.8
STD DEV	1.00	0.95	0.93	0.92	0.92

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor)
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 2 OF 4: CATEGORICAL CHANGE ANALYSIS, NUMBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND p-VALUE (d)
WEEK 2						
IMPROVED (b)	23(10%)	44(19%)	60(28%)	46(21%)	55(25%)	<0.001
NO CHANGE	187(85%)	179(79%)	151(69%)	171(79%)	161(74%)	
WORSENED (c)	12(5%)	5(2%)	7(3%)	0(0%)	2(<1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 6						
IMPROVED (b)	30(14%)	42(18%)	54(25%)	39(18%)	52(24%)	0.009
NO CHANGE	177(80%)	178(78%)	158(72%)	177(82%)	164(75%)	
WORSENED (c)	14(6%)	8(4%)	6(3%)	1(<1%)	2(<1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 12						
IMPROVED (b)	27(12%)	42(18%)	48(22%)	44(20%)	55(25%)	0.001
NO CHANGE	178(81%)	179(79%)	164(75%)	171(79%)	160(73%)	
WORSENED (c)	16(7%)	7(3%)	6(3%)	2(<1%)	3(1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

P-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.120	0.423	0.284	<0.001	0.997	0.931	0.273
WEEK 6:	0.001*	0.016*	0.035	0.119	0.753	0.181	<0.001	0.109	0.005	0.156
WEEK 12:	0.003*	0.001*	0.094	0.610	0.681	0.830	<0.001	0.094	0.285	0.229

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1
(c) Worsened is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Nonzero Correlation). Naproxen group was excluded
(e) Cochran-Mantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table A.34.2 Physician's Global Assessment-continued (Protocol 023)

PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 3 OF 4: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=210)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-0.4	-0.8	-1.0	-0.9	-1.0	<0.001	<0.001
STD DEV	0.88	0.92	0.91	0.87	0.90		
LS MEAN CHANGE (c)	-0.3	-0.8	-1.0	-0.9	-1.0		
WEEK 6							
OBSERVED MEAN CHANGE	-0.4	-0.7	-0.9	-0.9	-1.0	<0.001	<0.001
STD DEV	0.96	0.96	1.03	0.89	0.95		
LS MEAN CHANGE (c)	-0.4	-0.7	-0.8	-0.8	-0.9		
WEEK 12							
OBSERVED MEAN CHANGE	-0.3	-0.7	-0.8	-0.8	-0.9	<0.001	<0.001
STD DEV	0.94	0.97	1.02	0.92	0.98		
LS MEAN CHANGE (c)	-0.3	-0.6	-0.8	-0.8	-0.9		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e): 100MG BID VS. NAPROXEN; 200MG BID VS. NAPROXEN; 400MG BID VS. NAPROXEN

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.78 (0.65 to 0.93)	0.98 (0.83 to 1.15)	0.89 (0.75 to 1.05)
WEEK 6:	0.75 (0.60 to 0.92)	0.89 (0.73 to 1.08)	0.88 (0.73 to 1.07)
WEEK 12:	0.73 (0.58 to 0.92)	0.88 (0.71 to 1.08)	0.91 (0.73 to 1.12)

p-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY: 200MG BID VS. PLACEBO	PRIMARY: 400MG BID VS. PLACEBO	SECONDARY: 100MG BID VS. PLACEBO	SECONDARY: 200MG BID VS. 100MG BID	SECONDARY: 400MG BID VS. 100MG BID	SECONDARY: 400MG BID VS. 200MG BID	SECONDARY: NAPROXEN VS. PLACEBO	SECONDARY: NAPROXEN VS. 100MG BID	SECONDARY: NAPROXEN VS. 200MG BID	SECONDARY: NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.089	0.154	0.244	<0.001	0.004	0.790	0.153
WEEK 6:	<0.001*	<0.001*	<0.001	0.113	0.121	0.972	<0.001	0.004	0.205	0.193
WEEK 12:	<0.001*	<0.001*	<0.001	0.135	0.070	0.750	<0.001	0.005	0.199	0.334

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 0.787 for week 2, 0.868 for week 6, 0.883 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.35.1 Patient's Global Assessment (Protocol 023)

TABLE 17
PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	p
BASELINE						
N	221	228	218	217	218	
MEAN	3.7	3.7	3.7	3.7	3.7	
STD DEV	0.68	0.67	0.66	0.64	0.63	
WEEK 2						
N	221	228	218	217	218	
MEAN	3.4	2.9	2.7	2.7	2.7	
STD DEV	0.96	0.98	0.88	0.82	0.83	
WEEK 6						
N	221	228	218	217	218	
MEAN	3.4	3.0	3.0	2.9	2.8	
STD DEV	1.04	0.96	1.00	0.96	0.94	
WEEK 12						
N	221	228	218	217	218	
MEAN	3.4	3.1	2.9	3.0	2.8	
STD DEV	1.05	0.98	0.98	0.93	0.94	

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor)
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 2 OF 4: CATEGORICAL CHANGE ANALYSIS, NUMBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND p-VALUE (d)
WEEK 2						
IMPROVED (b)	24(11%)	49(21%)	54(25%)	61(28%)	61(28%)	<0.001
NO CHANGE	183(83%)	174(76%)	158(72%)	152(70%)	154(71%)	
WORSENED (c)	14(6%)	5(2%)	6(3%)	4(2%)	3(1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 6						
IMPROVED (b)	27(12%)	44(19%)	54(25%)	45(21%)	53(26%)	0.001
NO CHANGE	176(80%)	177(78%)	156(72%)	168(77%)	160(73%)	
WORSENED (c)	18(8%)	7(3%)	8(4%)	4(2%)	5(2%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 12						
IMPROVED (b)	29(13%)	40(18%)	50(23%)	41(19%)	57(26%)	0.007
NO CHANGE	171(77%)	180(79%)	160(73%)	169(78%)	157(72%)	
WORSENED (c)	21(10%)	8(4%)	8(4%)	7(3%)	4(2%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

p-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.688	0.171	0.335	<0.001	0.999	0.352	0.959
WEEK 6:	0.001*	0.001*	0.004	0.376	0.742	0.616	<0.001	0.217	0.826	0.371
WEEK 12:	0.002*	0.007*	0.016	0.294	0.613	0.411	<0.001	0.026	0.302	0.080

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1
(c) Worsened is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Monzero Correlation). Naproxen group was excluded
(e) Cochran-Mantel-Haenszel test of treatment comparisons stratified by center (Row Mean Scores Differ)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table A.35.2 Patient's Global Assessment-continued (Protocol 023)

TABLE 17
PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 3 OF 4: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL P-VALUE(c)	LINEAR TREND P-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-0.4	-0.8	-1.0	-1.0	-1.0	<0.001	<0.001
STD DEV	0.93	0.99	0.99	0.99	0.91		
LS MEAN CHANGE (c)	-0.3	-0.8	-1.0	-1.0	-1.0		
WEEK 6							
OBSERVED MEAN CHANGE	-0.4	-0.7	-0.8	-0.8	-0.9	<0.001	<0.001
STD DEV	0.96	0.99	1.04	0.95	0.99		
LS MEAN CHANGE (c)	-0.3	-0.7	-0.8	-0.8	-0.9		
WEEK 12							
OBSERVED MEAN CHANGE	-0.3	-0.6	-0.8	-0.7	-0.9	<0.001	<0.001
STD DEV	0.97	0.97	1.01	0.96	1.00		
LS MEAN CHANGE (c)	-0.3	-0.6	-0.8	-0.7	-0.9		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.78 (0.64 to 0.93)	0.95 (0.81 to 1.12)	0.94 (0.80 to 1.11)
WEEK 6:	0.75 (0.59 to 0.94)	0.92 (0.74 to 1.13)	0.88 (0.70 to 1.08)
WEEK 12:	0.66 (0.50 to 0.86)	0.89 (0.71 to 1.12)	0.82 (0.65 to 1.04)

P-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.024	0.012	0.913	<0.001	0.004	0.548	0.478
WEEK 6:	<0.001*	<0.001*	<0.001	0.001	0.197	0.656	<0.001	0.010	0.405	0.201
WEEK 12:	<0.001*	<0.001*	0.001	0.024	0.122	0.479	<0.001	<0.001	0.304	0.083

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate.
the corresponding ROOT MSE are: 0.826 for week 2, 0.914 for week 6, 0.909 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.36.1 Number of Tender/Painful Joints (Protocol 022)

M49-96-02-022

TABLE 20
NUMBER OF TENDER/PAINFUL JOINTS
PART 1 OF 5: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=240)	SC-58635 200MG BID (N=235)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=225)
BASELINE					
N	231	240	235	217	225
MEAN	29.7	29.6	31.0	26.2	29.3
STD DEV	14.84	14.94	15.24	14.31	14.22
WEEK 6					
N	231	240	235	217	225
MEAN	21.9	18.5	18.8	16.9	18.6
STD DEV	15.63	15.26	15.77	14.36	15.20
WEEK 9					
N	231	240	235	217	225
MEAN	20.8	18.5	18.7	16.5	18.2
STD DEV	16.65	16.39	15.71	14.69	15.35
WEEK 12					
N	231	240	235	217	225
MEAN	21.1	17.9	18.6	16.5	18.8
STD DEV	17.27	16.04	16.24	14.96	16.06

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 68 with lower score as better

NUMBER OF TENDER/PAINFUL JOINTS
PART 2 OF 5: PATIENT'S OVERALL STATUS IN CHANGE FROM BASELINE. NUMBER OF PATIENTS (%) (a)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 231)	SC-58635 100MG BID (N 240)	SC-58635 200MG BID (N 235)	SC-58635 400MG BID (N 217)	NAPROXEN 500MG BID (N 225)	LINEAR TREND P VALUE (d)
WEEK 6						
IMPROVED (b)	72(31%)	104(43%)	112(48%)	103(47%)	102(45%)	0.001
NO CHANGE	149(64%)	129(54%)	116(49%)	106(49%)	112(50%)	
WORSENED (c)	10(4%)	7(3%)	7(3%)	8(4%)	11(5%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK 9						
IMPROVED (b)	89(39%)	110(46%)	108(46%)	109(50%)	106(47%)	0.004
NO CHANGE	126(55%)	107(45%)	122(52%)	104(48%)	105(47%)	
WORSENED (c)	16(7%)	15(6%)	5(2%)	4(2%)	12(5%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK 12						
IMPROVED (b)	88(38%)	127(53%)	115(49%)	106(49%)	98(44%)	0.014
NO CHANGE	126(55%)	96(40%)	112(48%)	105(48%)	112(50%)	
WORSENED (c)	17(7%)	17(7%)	8(3%)	6(4%)	15(7%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	

P-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY		SECONDARY						
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 6:	0.001*	0.001*	0.062	0.354	0.277	0.945	0.001	0.569	0.662	0.733
WEEK 9:	0.004*	0.001*	0.017	0.804	0.497	0.414	0.031	0.784	0.782	0.496
WEEK 12:	0.001*	0.015*	0.062	0.751	0.783	0.754	0.225	0.091	0.105	0.264

(a) This table is based on the last observation carried forward approach
(b) [illegible] used in defining as number of improved joints minus number of worsened joints is larger than or equal to 50% of the number of joints with baseline score > 0
(c) Worsened is defined as number of worsened joints minus number of improved joints is larger than or equal to 50% of the number of joints with baseline score > 0
(d) Cochran-Mantel-Haenszel test : linear dose trend stratified by center (Modified Ridit Scores). Naproxen dose was excluded
(e) Cochran-Mantel-Haenszel test on treatment comparison stratified by center (Row Mean Scores Differ)

Table A.36.2 Number of Tender/Painful Joints-(Protocol 022)

PART 3 OF 5: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=240)	SC-58635 200MG BID (N=235)	SC-58635 400MG BID (N=237)	NAPROXEN 500MG BID (N=225)	OVERALL P-VALUE(c)	LINEAR TREND P-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-7.0	-11.0	-12.2	-11.3	-10.2	<0.001	<0.001
STD DEV	12.50	12.26	12.77	11.68	11.67		
LS MEAN CHANGE (c)	-7.5	-11.3	-12.0	-11.8	-10.6		
WEEK 6							
OBSERVED MEAN CHANGE	-8.0	-11.1	-12.3	-11.7	-10.1	<0.001	<0.001
STD DEV	14.75	14.18	13.04	12.53	12.59		
LS MEAN CHANGE (c)	-8.2	-11.3	-11.9	-12.2	-10.5		
WEEK 12							
OBSERVED MEAN CHANGE	-7.6	-11.6	-12.4	-11.7	-9.5	<0.001	<0.001
STD DEV	14.27	14.16	13.99	13.59	13.16		
LS MEAN CHANGE (c)	-6.2	-12.0	-12.3	-12.4	-10.1		

D RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	1.05 (0.87 to 1.27)	1.11 (0.92 to 1.34)	1.11 (0.92 to 1.34)
WEEK 6:	1.07 (0.87 to 1.33)	1.13 (0.92 to 1.40)	1.16 (0.94 to 1.42)
WEEK 12:	1.19 (0.96 to 1.49)	1.22 (0.98 to 1.52)	1.23 (0.99 to 1.54)

P-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY		SECONDARY						
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.511	0.535	0.982	0.001	0.607	0.247	0.248
WEEK 6:	0.001*	<0.001*	0.005	0.601	0.450	0.808	0.045	0.493	0.232	0.156
WEEK 12:	<0.001*	<0.001*	0.001	0.732	0.736	0.934	0.303	0.104	0.069	0.055

(a) This table is based on the last observation carried forward approach
(b) Scale ranges from 0 to 28 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate.
The corresponding ADJUSTED MEANS are: 11.003 for week 2, 12.177 for week 6, 12.595 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) "RATIO" is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.37.1 Number of Swollen Joints (Protocol 023)

TABLE 19
NUMBER OF SWOLLEN JOINTS
PART 1 OF 5: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	221	228	218	217	218
MEAN	19.7	20.6	21.2	20.5	20.6
STD DEV	11.95	11.77	11.69	10.93	12.00
WEEK 2					
N	221	228	218	217	218
MEAN	16.8	13.7	13.6	13.7	13.4
STD DEV	12.73	10.78	11.10	9.18	10.22
WEEK 6					
N	221	228	218	217	218
MEAN	15.8	13.8	14.3	13.5	13.6
STD DEV	13.43	10.67	13.21	9.59	11.32
WEEK 12					
N	221	228	218	217	218
MEAN	16.0	13.9	14.4	13.6	13.9
STD DEV	13.39	10.81	12.26	9.47	11.76

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 66 with lower score as better
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

NUMBER OF SWOLLEN JOINTS
PART 2 OF 5: PATIENT'S OVERALL STATUS IN CHANGE FROM BASELINE, NUMBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND P-VALUE (d)
WEEK 2						
IMPROVED (b)	66(30%)	72(32%)	89(41%)	68(31%)	86(39%)	0.191
NO CHANGE	136(62%)	147(64%)	120(55%)	142(65%)	127(58%)	
WORSENED (c)	19(9%)	9(4%)	9(4%)	7(3%)	5(2%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 6						
IMPROVED (b)	81(37%)	76(33%)	98(45%)	76(35%)	93(43%)	0.324
NO CHANGE	117(53%)	144(63%)	121(56%)	132(61%)	117(54%)	
WORSENED (c)	23(10%)	8(4%)	7(3%)	9(4%)	8(4%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 12						
IMPROVED (b)	67(30%)	73(32%)	90(41%)	76(34%)	92(42%)	0.069
NO CHANGE	133(60%)	145(64%)	119(55%)	134(62%)	113(52%)	
WORSENED (c)	21(10%)	10(4%)	9(4%)	9(4%)	13(6%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

P-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	0.003*	0.468	0.385	0.054	0.079	0.022	0.010	0.095	0.764	0.065
WEEK 6:	0.033	0.896	0.931	0.033	0.653	0.381	0.051	0.047	0.982	0.081
WEEK 12:	0.002*	0.269	0.926	0.024	0.781	0.083	0.007	0.074	0.669	0.148

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as number of improved joints minus number of worsened joints is larger than or equal to 50% of the number of joints with baseline score > 0
(c) Worsened is defined as number of worsened joints minus number of improved joints is larger than or equal to 50% of the number of joints with baseline score > 0
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Ridit Correlation). Naproxen group was excluded
(e) Cochran-Mantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table A.37.2 Number of Swollen Joints (Protocol 023)

NUMBER OF SWOLLEN JOINTS
PART 3 OF 5: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL P-VALUE(c)	LINEAR TREND P-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-3.8	-6.3	-7.6	-6.8	-7.2		
STD DEV	9.23	8.32	9.57	8.18	9.08		
LS MEAN CHANGE (c)	-3.9	-6.3	-7.1	-6.6	-6.8		
WEEK 6						0.003	0.001
OBSERVED MEAN CHANGE	-3.9	-6.2	-7.0	-6.9	-7.0		
STD DEV	10.01	9.46	9.42	8.98	8.99		
LS MEAN CHANGE (c)	-3.8	-5.9	-6.2	-6.4	-6.4		
WEEK 12						0.006	0.002
OBSERVED MEAN CHANGE	-3.7	-6.0	-6.8	-6.9	-6.6		
STD DEV	10.40	9.61	9.78	8.67	10.05		
LS MEAN CHANGE (c)	-3.7	-5.9	-6.0	-6.4	-6.1		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.92 (0.74 to 1.15)	1.04 (0.85 to 1.29)	0.96 (0.77 to 1.20)
WEEK 6:	0.93 (0.71 to 1.20)	0.97 (0.75 to 1.25)	1.00 (0.77 to 1.29)
WEEK 12:	0.97 (0.73 to 1.28)	0.99 (0.75 to 1.31)	1.04 (0.79 to 1.37)

P-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY		SECONDARY						
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.344	0.698	0.463	<0.001	0.453	0.681	0.721
WEEK 6:	0.002*	0.001*	0.006	0.725	0.563	0.822	<0.001	0.546	0.803	0.981
WEEK 12:	0.004*	0.001*	0.006	0.866	0.582	0.706	0.003	0.818	0.952	0.751

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 66 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate.
the corresponding ROOT MSE are: 7.375 for week 2, 8.151 for week 6, 8.456 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.38.1 ACR-20 Responder Index (Protocol 023-ITT)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
P49-96-02-023

TABLE 16
CATEGORIAL STATUS BASED ON THE ACR RESPONDERS INDEX (20%) (a)
NUMBER OF PATIENTS (%)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND P-VALUE (c)
WEEK2						
IMPROVED (b)	55(25%)	95(42%)	101(46%)	93(43%)	97(44%)	<0.001
NOT IMPROVED	166(75%)	133(58%)	117(54%)	124(57%)	121(56%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK6						
IMPROVED (b)	60(27%)	87(38%)	89(41%)	94(43%)	101(46%)	<0.001
NOT IMPROVED	161(73%)	141(62%)	129(59%)	123(57%)	117(54%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK12						
IMPROVED (b)	50(23%)	68(30%)	86(39%)	79(36%)	91(42%)	<0.001
NOT IMPROVED	171(77%)	160(70%)	132(61%)	138(64%)	127(58%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK2 :	<0.001*	<0.001*	<0.001	0.361	0.835	0.348	<0.001	0.537	0.698	0.507
WEEK6 :	0.002*	<0.001*	0.015	0.587	0.299	0.661	<0.001	0.096	0.294	0.507
WEEK12 :	<0.001*	0.002*	0.060	0.038	0.198	0.432	<0.001	0.011	0.585	0.242

Note: The ITT cohort includes only patients who had at least one dose of study medication
(a) This table is based on the last observation carried forward approach
(b) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index
(c) Cochran-Mantel-Haenszel test of linear dose trend stratified by center, p-value for Monsero Correlation, naproxen was excluded
(d) Cochran-Mantel-Haenszel test of treatment comparison stratified by center, p-value for Row Mean Scores Differ
* Statistically significant according to the Hochberg Procedure(primary pairwise comparisons only)

Table A.38.2 ACR-20 Responder Index (Protocol 022, ITT)

SC-58635 COMPARATIVE EFFICACY AND GI SAFETY VS NAPROXEN IN RA
M65-96-02 022

TABLE 18
CATEGORICAL STATUS BASED ON THE ACR RESPONDERS INDEX (20%) (a)
NUMBER OF PATIENTS (%)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=240)	SC-58635 200MG BID (N=235)	SC-58635 400MG BID (N=237)	NAPROXEN 500MG BID (N=225)	LINEAR TREND P-VALUE (c)
WEEK2						
IMPROVED (b)	51(22%)	95(40%)	115(49%)	89(41%)	89(40%)	<0.001
NOT IMPROVED	180(78%)	145(60%)	120(51%)	128(59%)	136(60%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK6						
IMPROVED (b)	64(28%)	93(39%)	114(49%)	97(45%)	88(39%)	<0.001
NOT IMPROVED	167(72%)	147(61%)	121(51%)	120(55%)	137(61%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK12						
IMPROVED (b)	66(29%)	99(41%)	107(46%)	85(39%)	81(36%)	0.005
NOT IMPROVED	165(71%)	141(59%)	128(54%)	132(61%)	144(64%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	PRIMARY		SECONDARY					
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK2 :	<0.001*	<0.001*	<0.001	0.060	0.586	0.160	<0.001	0.868	0.026	0.561
WEEK6 :	<0.001*	0.005*	0.008	0.035	0.693	0.047	0.018	0.817	0.011	0.578
WEEK12 :	<0.001*	0.012*	0.005	0.273	0.956	0.320	0.049	0.665	0.070	0.562

(a) This table is based on the last observation carried forward approach
(b) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index
(c) Cochran-Mantel-Haenszel test of linear dose trend stratified by center, p-value for Nonzero Correlation, narrowen was excluded
(d) Cochran-Mantel-Haenszel test of treatment comparison stratified by center, p-value for Row Mean Scores Diffe
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.38.3 ACR-20 Responder Index (Protocol 023-Evaluable)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS CAPSICUM IN RA
[illegible]

APPENDIX [illegible]
CATEGORICAL STATUS BASED ON THE ACR RESPONDABLE INDEX (20%)
NUMBER OF PATIENTS (%)

EVALUABLE COHORT

	PLACEBO (N 231)*	SC-58635 100MG BID (N:228)*	SC-58635 200MG BID (N 219)*	SC-58635 400MG BID (N:217)*	NAPROXEN 500MG BID (N 216)*	LINEAR TREND P VALUE (b)
WEEK [illegible]						
IMPROVED (a)	40(30%)	85(46%)	84(47%)	82(47%)	92(51%)	0.015
NOT IMPROVED	95(70%)	98(54%)	94(53%)	93(53%)	87(49%)	
TOTAL	135(100%)	183(100%)	178(100%)	175(100%)	179(100%)	
WEEK 6						
IMPROVED (a)	38(51%)	65(54%)	68(52%)	78(61%)	95(60%)	0.080
NOT IMPROVED	36(49%)	56(46%)	64(48%)	50(39%)	56(40%)	
TOTAL	74(100%)	121(100%)	132(100%)	128(100%)	161(100%)	
WEEK 12						
IMPROVED (a)	27(46%)	46(46%)	64(63%)	65(65%)	69(63%)	0.033
NOT IMPROVED	32(54%)	53(54%)	38(37%)	43(40%)	41(37%)	
TOTAL	59(100%)	99(100%)	102(100%)	108(100%)	110(100%)	
FINAL						
IMPROVED (a)	46(33%)	[illegible]	83(44%)	95(49%)	93(49%)	0.001
NOT IMPROVED	95(67%)	[illegible]	104(56%)	97(50%)	96(51%)	
TOTAL	141(100%)	193(100%)	187(100%)	192(100%)	189(100%)	

P-VALUE FOR TREATMENT COMPARISONS (c):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	600MG BID VS. 200MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK [illegible]	0.019	0.021	0.018	0.769	0.850	0.900	[illegible]	0.338	0.273	0.354
WEEK 6	0.611	0.564	0.103	0.810	0.147	0.155	0.044	0.360	0.265	0.352
WEEK 12	0.641	0.139	0.239	0.033	0.049	0.526	0.029	0.014	0.980	0.664
FINAL	0.008	0.039	0.019	0.136	0.045	0.647	0.704	0.737	0.369	0.983

* (a) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability
(b) Cochran-Mantel-Haenszel test of linear dose trend stratified by center. p value for Kendall's Correlation, naproxen was excluded
(c) Cochran-Mantel-Haenszel test of treatment comparison stratified by center. p value for Row Mean Scores Differ
* All randomized patients

Table A.39.1 ACR-50 Responder Index (Protocol 022-ITT)

SC-58635 COMPARATIVE EFFICACY BID DGI SAFETY VS NAPROXEN IN RA
M69 96-02-022

TABLE 31
CATEGORICAL STATUS BASED ON THE ACR RESPONDERS INDEX (50%) (a)
NUMBER OF PATIENTS (%)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N 240)	SC-58635 200MG BID (N 235)	SC-58635 400MG BID (N 217)	NAPROXEN 500MG BID (N=225)	LITREAR TREND P VALUE (c)
WEEK4						
IMPROVED (b)	14(6%)	22(9%)	35(15%)	34(16%)	26(12%)	<0.001
NOT IMPROVED	217(94%)	218(91%)	200(85%)	183(84%)	197(88%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK8						
IMPROVED (b)	16(8%)	29(12%)	40(17%)	36(17%)	29(13%)	<0.001
NOT IMPROVED	213(92%)	211(88%)	195(83%)	181(83%)	196(87%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK12						
IMPROVED (b)	17(7%)	26(11%)	41(17%)	36(17%)	29(13%)	<0.001
NOT IMPROVED	214(93%)	214(89%)	194(83%)	181(83%)	196(87%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK4	<0.001	0.001	0.228	0.047	0.024	0.698	0.009	0.161	0.434	0.317
WEEK8	0.001	0.005	0.180	0.061	0.135	0.676	0.041	0.692	0.147	0.276
WEEK12	<0.001	0.002	0.195	0.034	0.086	0.819	0.062	0.368	0.129	0.314

(a) Data fail-in is based on the last observation carried forward approach.
(b) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of
swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments:
1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) WAL Functional Disability
(c) [illegible] Mantel-Haenszel test of linear dose trend stratified by center. p value for Ranzers Correlation. Naproxen was excluded
(d) [illegible] Mantel-Haenszel test of treatment comparison stratified by center. p-value for Row Mean Scores Diff-r

Table A.39.2 ACR-50 Responder Index (Protocol 023-ITT)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
M69-96-02-023

TABLE 29
CATEGORIAL STATUS BASED ON THE ACR RESPONDERS INDEX (50%) (a)
NUMBER OF PATIENTS (%)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND P-VALUE (c)
WEEK4						
IMPROVED (b)	12(5%)	24(11%)	37(17%)	27(12%)	33(15%)	0.004
NOT IMPROVED	209(95%)	202(89%)	181(83%)	190(88%)	185(85%)	
TOTAL	221(100%)	226(100%)	218(100%)	217(100%)	218(100%)	
WEEK8						
IMPROVED (b)	15(7%)	22(10%)	35(16%)	25(12%)	32(15%)	0.008
NOT IMPROVED	206(93%)	206(90%)	183(84%)	192(88%)	186(85%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK12						
IMPROVED (b)	13(6%)	23(10%)	38(17%)	27(12%)	39(18%)	0.007
NOT IMPROVED	208(94%)	205(90%)	180(83%)	190(88%)	179(82%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK4	<0.001	0.010	0.029	0.135	0.795	0.142	<0.001	0.275	0.423	0.324
WEEK8	0.001	0.046	0.245	0.082	0.583	0.147	0.006	0.211	0.702	0.269
WEEK12	<0.001	0.017	0.061	0.030	0.519	0.111	<0.001	0.024	0.619	0.125

Note: The [illegible] include only patients who had at least one dose of study medication.

a: This table is based on the last observation carried forward approach

b: IMPROVED: At least 20% improvement from baseline in the number of tender/painful joints and in the number of [illegible] as well as at least 50% improvement from baseline in at least three of the following assessments: [illegible] at a Clinic; 2) Patient's Global; 3) Patient's Assessment of Pain; 4) C-Reactive Protein; 5) HAQ Functional Disability [illegible]

c: Cochran-Mantel-Haenszel test of linear dose trend stratified by center. p-value for Nonzero Correlation. Response was ordinal

d: Cochran-Mantel-Haenszel test of treatment comparison stratified by center. p-value for Row Mean Scores Differ

Table A.40 Patient's Assessment of Arthritis Pain-VAS (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
M49-96-02-023

TABLE 21
PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	220	228	216	216	218
MEAN	68.1	66.1	67.8	67.8	66.8
STD DEV	19.57	20.13	19.98	19.78	18.48
WEEK 2					
N	220	228	218	217	218
MEAN	58.7	49.8	61.4	62.2	60.6
STD DEV	27.15	26.25	25.10	24.62	24.36
WEEK 6					
N	221	228	218	217	218
MEAN	60.5	47.8	46.5	45.6	43.7
STD DEV	27.86	27.74	28.38	26.39	25.77
WEEK 12					
N	221	228	218	217	218
MEAN	61.0	51.0	47.0	48.7	44.6
STD DEV	27.88	28.61	29.03	26.48	27.43

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 mm with lower score as better
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL P-VALUE(c)	LINEAR TREND P-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-9.4	-20.3	-26.5	-25.6	-26.2		
STD DEV	25.81	24.27	24.12	23.61	25.02		
LS MEAN CHANGE (c)	-8.8	-20.7	-26.8	-25.1	-26.1		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-7.4	-18.3	-21.4	-22.2	-23.1		
STD DEV	25.59	25.94	28.00	27.60	26.35		
LS MEAN CHANGE (c)	-6.1	-18.3	-20.4	-21.2	-22.5		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-6.1	-15.1	-20.9	-19.0	-22.1		
STD DEV	25.07	26.83	28.12	27.18	27.77		
LS MEAN CHANGE (c)	-5.5	-15.5	-20.4	-18.5	-22.0		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.79 (0.65 to 0.96)	1.00 (0.84 to 1.18)	0.96 (0.80 to 1.14)
WEEK 6:	0.81 (0.63 to 1.03)	0.90 (0.72 to 1.14)	0.94 (0.75 to 1.17)
WEEK 12:	0.71 (0.53 to 0.93)	0.93 (0.73 to 1.18)	0.84 (0.65 to 1.07)

P-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.014	0.046	0.655	<0.001	0.012	0.962	0.620
WEEK 6:	<0.001	<0.001	<0.001	0.380	0.233	0.753	<0.001	0.073	0.364	0.555
WEEK 12:	<0.001	<0.001	<0.001	0.042	0.236	0.418	<0.001	0.007	0.519	0.146

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 22.76 for week 2, 24.84 for week 6, and 25.95 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.41 C-Reactive Protein (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
049-96-02-023

TABLE 26.1
C-REACTIVE PROTEIN
PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=220)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	215	222	214	210	218
MEAN	15572.1	16464.0	17887.9	18590.5	18481.0
STD DEV	15608.12	19090.11	20419.69	15790.92	18677.37
WEEK 2					
N	220	220	218	216	217
MEAN	15154.5	16592.1	17367.0	16935.2	14023.0
STD DEV	16015.79	20979.44	20191.55	17566.80	14229.62
WEEK 6					
N	221	228	218	217	218
MEAN	16478.6	17693.0	17243.1	18838.7	14504.6
STD DEV	18308.60	22025.47	19269.29	20799.01	15386.34
WEEK 12					
N	221	228	218	217	218
MEAN	18040.7	16077.2	16825.7	17963.1	13756.9
STD DEV	27587.43	20610.35	18969.70	19711.54	13783.06

(a) This table is based on the last observation carried forward approach
(b) Unit of measurement : ug/L
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

C-REACTIVE PROTEIN
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=220)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL P-VALUE(c)	LINEAR TREND P-VALUE(d)
WEEK 2						0.168	0.159
OBSERVED MEAN CHANGE	-325.6	233.3	-359.8	1409.5	-1352.4		
STD DEV	12853.82	11978.74	19069.37	12330.92	12825.87		
LS MEAN CHANGE (c)	-300.7	703.6	374.8	1535.4	-1267.1		
WEEK 6						0.016	0.172
OBSERVED MEAN CHANGE	1904.7	1369.4	-562.1	3247.6	-823.8		
STD DEV	15781.95	13404.89	12134.44	15726.60	13705.46		
LS MEAN CHANGE (c)	1428.0	2106.5	395.5	3871.3	-240.8		
WEEK 12						0.040	0.912
OBSERVED MEAN CHANGE	2604.7	536.0	-967.3	2595.2	-1600.0		
STD DEV	26246.44	14431.49	14446.40	16625.43	12311.82		
LS MEAN CHANGE (c)	2778.4	1236.1	37.6	2990.0	-1269.8		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	-0.56 (NON-ESTIMABLE)	-0.30 (NON-ESTIMABLE)	-1.21 (NON-ESTIMABLE)
WEEK 6:	-6.18 (NON-ESTIMABLE)	-1.16 (NON-ESTIMABLE)	-11.4 (NON-ESTIMABLE)
WEEK 12:	-0.87 (NON-ESTIMABLE)	-0.83 (NON-ESTIMABLE)	-2.35 (NON-ESTIMABLE)

P-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	0.383	0.561	0.115	0.775	0.472	0.320	0.417	0.091	0.164	0.018
WEEK 6:	0.595	0.432	0.061	0.186	0.175	0.008	0.179	0.060	0.574	0.001
WEEK 12:	0.333	0.068	0.896	0.453	0.273	0.068	0.812	0.217	0.618	0.009

(a) This table is based on the last observation carried forward approach
(b) Unit of measurement : ug/L with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate. the corresponding ROOT MSE are: 11963 for week 2, 13440 for week 6, and 16562 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.42 HAQ Functional Disability Index (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
049-96-02-021

TABLE 25
HAQ FUNCTIONAL DISABILITY INDEX
PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	219	226	217	216	218
MEAN	1.4	1.4	1.3	1.3	1.4
STD DEV	0.68	0.70	0.67	0.63	0.68
WEEK 2					
N	221	228	218	217	218
MEAN	1.3	1.1	1.0	1.0	1.1
STD DEV	0.67	0.69	0.68	0.64	0.67
WEEK 6					
N	221	228	218	217	218
MEAN	1.3	1.2	1.1	1.0	1.1
STD DEV	0.72	0.71	0.72	0.66	0.69
WEEK 12					
N	221	228	218	217	218
MEAN	1.3	1.3	1.1	1.1	1.1
STD DEV	0.73	0.70	0.73	0.67	0.68

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 3 with lower score as less disability
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

HAQ FUNCTIONAL DISABILITY INDEX
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2							
OBSERVED MEAN CHANGE	-0.1	-0.2	-0.3	-0.3	-0.3	<0.001	<0.001
STD DEV	0.64	0.62	0.65	0.67	0.67		
LS MEAN CHANGE (c)	-0.1	-0.2	-0.3	-0.3	-0.3		
WEEK 6							
OBSERVED MEAN CHANGE	-0.1	-0.2	-0.3	-0.3	-0.3	<0.001	<0.001
STD DEV	0.69	0.63	0.51	0.52	0.60		
LS MEAN CHANGE (c)	-0.1	-0.2	-0.3	-0.3	-0.3		
WEEK 12							
OBSERVED MEAN CHANGE	-0.1	-0.1	-0.3	-0.3	-0.3	<0.001	<0.001
STD DEV	0.69	0.64	0.51	0.53	0.60		
LS MEAN CHANGE (c)	-0.1	-0.1	-0.3	-0.3	-0.3		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.83 (0.59 to 1.15)	1.00 (0.62 to 1.45)	1.05 (0.79 to 1.42)
WEEK 6:	0.69 (0.43 to 1.04)	1.07 (0.76 to 1.51)	0.99 (0.69 to 1.41)
WEEK 12:	0.96 (0.30 to 0.90)	0.94 (0.64 to 1.38)	0.98 (0.67 to 1.43)

p-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.080	0.124	0.837	<0.001	0.244	0.560	0.707
WEEK 6:	0.006	<0.001	<0.001	0.025	0.074	0.650	<0.001	0.065	0.698	0.956
WEEK 12:	0.183	<0.001	<0.001	0.031	0.017	0.813	<0.001	0.012	0.738	0.923

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 3 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 0.626 for week 2, 0.654 for week 6, and 0.662 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.43 Withdrawal-Lack of Arthritis Efficacy (Protocols 022, 023)

Text Table 40. Reasons for Study Termination (All Randomized Patients: 12-Week Pivotal Studies 022 and 023 and 12-Week Pooled Pivotal Studies)

	Number of Rheumatoid Arthritis Patients by Treatment Group				
		Celecoxib			Naproxen
Study	Placebo	100 mg BID	200 mg BID	400 mg BID	500 mg BID
Study 022	(n=231)	(n=240)	(n=235)	(n=218)[a]	(n=225)
Total Completed	101 (44%)	154 (64%)	158 (67%)	137 (63%)	138 (61%)
Total Withdrawn	130 (56%)	86 (36%)	77 (33%)	81 (37%)	87 (39%)
Lost to Follow-up	3 (1%)	1 (<1%)	3 (1%)	1(<1%)	1 (<1%)
Pre-Existing Violation	2 (<1%)	1 (<1%)	3 (1%)	2 (<1%)	0 (0%)
Protocol Non-Compliance	10 (4%)	4 (2%)	4 (2%)	7 (3%)	9 (4%)
Treatment Failure	104 (45%)	67 (28%)	50 (21%)	59 (27%)	65 (29%)
Adverse Event	11 (5%)	13 (5%)	17 (7%)	12 (6%)	12 (5%)
Study 023	(n=221)	(n=228)	(n=219)[a]	(n=217)	(n=218)
Total Completed	78(35%)	117 (51%)	124 (57%)	126 (58%)	133(61%)
Total Withdrawn	143 (65%)	111 (49%)	95 (43%)	91 (42%)	85(39%)
Lost to Follow-up	0 (0%)	0 (0%)	0 (0%)	2 (<1%)	0 (0%)
Pre-Existing Violation	2(<1%)	2 (<1%)	3 (1%)	2 (<1%)	0 (0%)
Protocol Non-Compliance	4 (2%)	5 (2%)	2 (<1%)	2 (<1%)	0 (0%)
Treatment Failure	125 (57%)	92 (40%)	74 (34%)	69 (32%)	69(32%)
Adverse Event	12 (5%)	12 (5%)	16 (7%)	16 (7%)	16 (7%)
Pooled[b]	(n=452)	(n=468)	(n=454)[a]	(n=435)[a]	(n=443)
Total Completed	179 (40%)	271 (58%)	282 (62%)	263 (60%)	271 (61%)
Total Withdrawn	273 (60%)	197 (42%)	172 (38%)	172 (40%)	172 (39%)
Lost to Follow-up	3 (<1%)	1 (<1%)	3 (<1%)	3 (<1%)	1 (<1%)
Pre-Existing Violation	4 (<1%)	3 (<1%)	6 (1%)	4 (<1%)	0 (0%)
Protocol Non-Compliance	14 (3%)	9 (2%)	6 (1%)	9 (2%)	9 (2%)
Treatment Failure	229 (51%)	159(34%)	124 (27%)	128 (29%)	134 (30%)
Adverse Event	23 (5%)	25 (5%)	33 (7%)	28 (6%)	28 (6%)

Derived from Individual Study Reports

a) Total number of patients includes two patients (one in the celecoxib 200 mg BID group [Study 023] and one in the celecoxib 400 mg BID group [Study 022]) who were randomized but did not receive study medication and are not included in the ITT Cohort.

b) Pooled represents data from combined pivotal Studies 022 and 023.

Table A.44 Time to Withdrawal - Lack of Arthritis Efficacy (023)

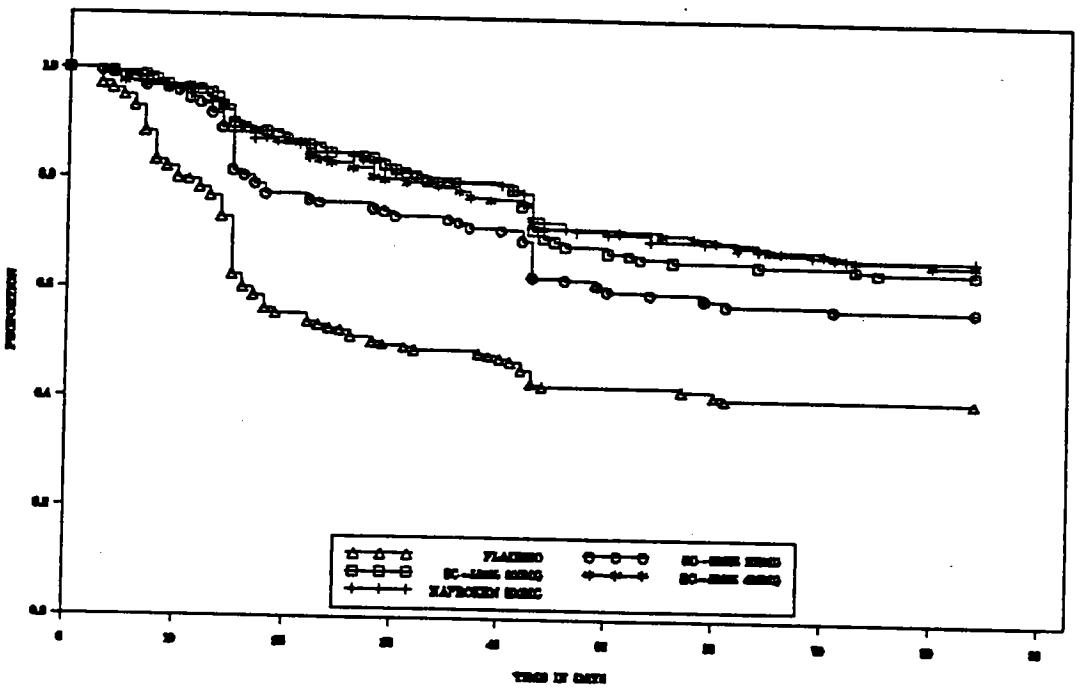


TABLE 20
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 2 OF 2: LOG-RANK TESTS FOR TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

p-VALUES FOR OVERALL COMPARISONS (a): <0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

100MG BID vs. PLACEBO	200MG BID vs. PLACEBO	400MG BID vs. PLACEBO	200MG BID vs. 100MG BID	400MG BID vs. 100MG BID	400MG BID vs. 200MG BID	NAPROXEN vs. PLACEBO	NAPROXEN vs. 100MG BID	NAPROXEN vs. 200MG BID	NAPROXEN vs. 400MG BID
<0.001	<0.001	<0.001	0.093	0.040	0.774	<0.001	0.035	0.647	0.670

(a) From log-rank test for all five treatment groups
(b) From pairwise log-rank test

Table A.45 Summary of Dosage change-OA /RA(protocol 024)

Table 9.7
Summary of Dosage Change: Long-Term Open Label Trial

024 Starting Dose	OA Withdrawals (N = 659)	OA Still Active (N = 1895)	OA Combined (N = 2554)
Celecoxib 100 mg BID			
NO CHANGES	193(29.3%)	469(24.7%)	662(25.9%)
INCREASE IN DOSE	444(67.4%)	1370(72.3%)	1816(71.0%)
100-200	437(66.3%)	1369(72.2%)	1806(70.7%)
100-300	3(0.5%)	1(< 0.1%)	4(0.2%)
100-400	2(0.3%)	0(0.0%)	2(< 0.1%)
OTHER	2(0.3%)	0(0.0%)	2(< 0.1%)
MULTIPLE CHANGES	22(3.3%)	56(3.0%)	78(3.1%)
100 200 100	13(2.0%)	26(1.4%)	39(1.5%)
100-200-100-200	4(0.6%)	21(1.1%)	25(1.0%)
100-200-100-200-100	1(0.2%)	0(0.0%)	1(< 0.1%)
100-200-100-other-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100 200 300 200	1(0.2%)	2(0.1%)	3(0.1%)
100-200-300-other-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100-200-other	1(0.2%)	1(< 0.1%)	2(< 0.1%)
100 200 other 100 200	1(0.2%)	0(0.0%)	1(< 0.1%)
100-200-other-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100-300-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100 other 200	1(0.2%)	2(0.1%)	3(0.1%)

'other' means celecoxib doses of 300 mg AM/200 mg PM, 200 mg AM/100 mg PM, 400 mg AM/300 mg PM, 200 mg QD, or 100 mg TID.

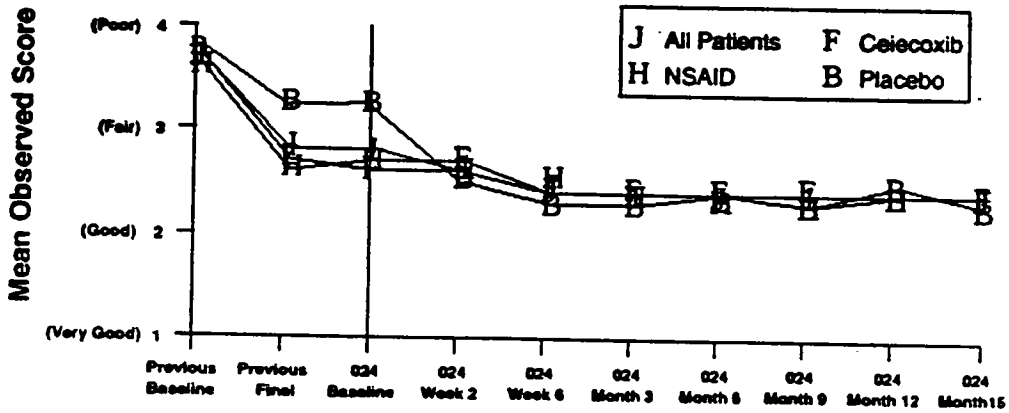
Table 9.7
Summary of Dosage Change: Long-Term Open Label Trial

024 Start Dose	RA Withdrawals (N = 523)	RA Still Active (N = 1422)	RA Combined (N = 1945)
Celecoxib 200 mg BID			
NO CHANGES	121(23.1%)	315(22.2%)	436(22.4%)
INCREASE IN DOSE	368(70.4%)	1023(71.9%)	1391(71.5%)
200-400	117(22.4%)	374(26.3%)	491(25.2%)
200-400	251(48.0%)	648(45.6%)	899(46.2%)
OTHER	0(0.0%)	1(< 0.1%)	1(< 0.1%)
DECREASE IN DOSE	4(0.8%)	5(0.4%)	9(0.5%)
MULTIPLE CHANGES	30(5.7%)	79(5.6%)	109(5.6%)
400-200-400	3(0.6%)	4(0.3%)	7(0.4%)
200-400-200-100	1(0.2%)	0(0.0%)	1(< 0.1%)
200-400-200-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200 400 200 300 400	2(0.4%)	1(< 0.1%)	3(0.2%)
200-400-200-400	1(0.2%)	0(0.0%)	1(< 0.1%)
200-400-300-400-200	1(0.2%)	0(0.0%)	1(< 0.1%)
200 400 400 200	1(0.2%)	0(0.0%)	1(< 0.1%)
200-400-100-200-100	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-400-400-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200 300 100	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-400-300	7(1.3%)	19(1.3%)	26(1.3%)
200-300-200-300	0(0.0%)	5(0.4%)	5(0.3%)
200-300-200-300-200	0(0.0%)	2(0.1%)	2(0.1%)
200 300 300-300 400	0(0.0%)	3(0.2%)	3(0.2%)
200-300-200-400-300-400-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-300-400-100-200-300-400	1(0.2%)	0(0.0%)	1(< 0.1%)
200 300 400 200	3(0.4%)	3(0.2%)	5(0.3%)
200-300-400-200-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-300-400-200-300-400	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200 300 400 200 400	0(0.0%)	2(0.1%)	2(0.1%)
200-300-400-200-other-100-other-200-300	1(0.2%)	0(0.0%)	1(< 0.1%)
200-300-400-300	7(1.3%)	11(0.8%)	18(0.9%)

'other' means celecoxib doses of 300 mg AM/200 mg PM, 200 mg AM/100 mg PM, 400 mg AM/300 mg PM, 100 mg QD, or 300 mg TID.

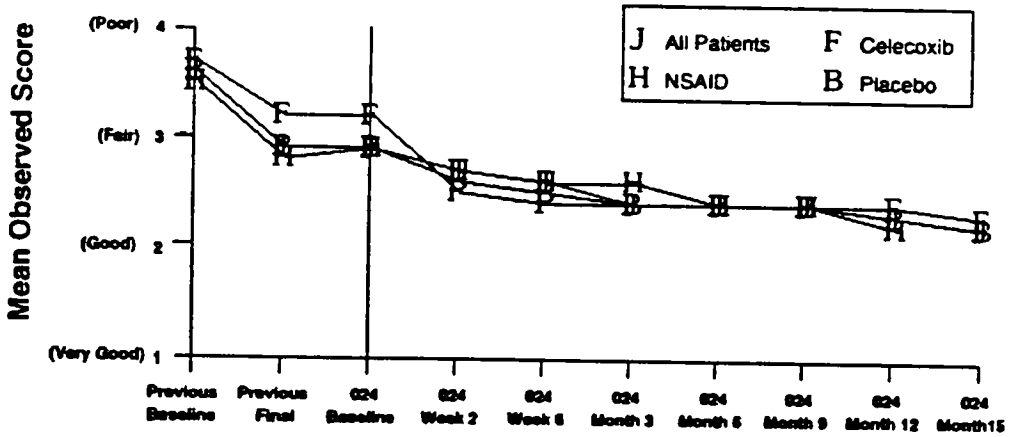
Figure A.1 Patient's Global Assessment-OA/RA (protocol 024)

Figure 7. **Patient's Global Assessment of Arthritic Condition: OA Patients (Study 024)**



All 2554	2554	2549	2453	2109	1602	990	665	270	84
Celecoxib 1579	1579	1578	1534	1341	1017	629	433	179	57
NSAID 503	502	501	469	349	247	153	89	26	0
Placebo 472	472	470	450	419	338	208	143	65	17

Figure 10. **Patient's Global Assessment of Arthritic Condition: RA Patients (Study 024)**



All 1945	1945	1943	1885	1689	1439	1089	722	294	111
Celecoxib 1197	1197	1197	1155	1039	890	672	455	193	78
NSAID 360	360	360	331	280	235	163	99	18	0
Placebo 388	388	386	379	350	314	254	168	83	33

Table A.46 Number of Treated/Unique Patients (All NDA trials)

Table 2.9
Summary of Treated Subjects/Patients: All Trials

	Placebo	Celecoxib 5-50 mg	Celecoxib 100 mg	Celecoxib 200 mg QD	Celecoxib 200 mg	Celecoxib 300 mg	Celecoxib 400 mg	Celecoxib 600-1200 mg	Celecoxib + Other Drug	Active Control or Other Drug
PHASE I - SINGLE DOSE(a)	35	36	35	0	149	10	13	35	0	[illegible]
PHASE I - MULTIPLE DOSE(a)	97	16	32	66	158	0	106	20	0	108
PHASE I - DRUG INTERACTION(a)	126	0	0	65	92	0	0	0	123	138
PHASE I - HEPATIC(a)	0	0	48	0	0	0	0	0	0	0
PHASE I - RENAL(a)	25	0	0	0	23	0	0	0	0	27
ARTHRITIS - OA	1329	863	1657	453	1208	0	99	0	0	1729
ARTHRITIS - RA	535	80	468	0	1032	0	516	0	0	1039
ARTHRITIS - LONG-TERM OPEN LABEL	0	0	2554	0	1845	0	0	0	0	0
ANALGESIA - DENTAL PAIN(b)	305	135	155	0	156	0	85	0	0	184
ANALGESIA - SURGICAL PAIN(c)	100	0	113	0	104	0	0	0	0	104
COMBINED STUDIES	2650	1130	5062	584	4487	10	819	55	123	3343

Note: 5-50 mg = 5, 20, 25, 40, or 50 mg, 600-1200 mg = 600, 800, 900, or 1200 mg.
All celecoxib regimens are BID unless otherwise specified.
(a) See Table 1.1 for description of regimens.
(b) See Table 1.4 for description of regimens.
(c) See Table 1.5 for description of regimens.

Table 2.10
Summary of Uniquely Treated Subjects/Patients: All Trials

	Placebo	Celecoxib 5-50 mg	Celecoxib 100 mg	Celecoxib 200 mg QD	Celecoxib 200 mg	Celecoxib 300 mg	Celecoxib 400 mg	Celecoxib 600-1200 mg	Celecoxib + Other Drug	Active Control or Other Drug
PHASE I - SINGLE DOSE(b)	35	36	35	0	149	10	13	35	0	0
PHASE I - MULTIPLE DOSE(b)	91	16	32	66	79	0	57	20	0	75
PHASE I - DRUG INTERACTION(b)	2	0	0	36	78	0	0	0	17	1
PHASE I - HEPATIC(b)	0	0	48	0	0	0	0	0	0	0
PHASE I - RENAL(b)	24	0	0	0	23	0	0	0	0	26
ARTHRITIS - OA	748	852	1612	398	1195	0	84	0	0	1176
ARTHRITIS - RA	350	80	463	0	1028	0	514	0	0	683
ARTHRITIS - LONG-TERM OPEN LABEL	0	0	993	0	764	0	0	0	0	0
ANALGESIA - DENTAL PAIN(b)	304	135	155	0	156	0	85	0	0	183

Note: 5-50 mg = 5, 20, 25, 40, or 50 mg, 600-1200 mg = 600, 800, 900, or 1200 mg.
All 20-56695 regimens are BID unless otherwise specified.
- Unique = each individual is only counted once. Subjects/patients who participated in multiple periods of a cross-over study or were treated in more than one study are only counted once. Thus, when a subject/patient participated in two different types of studies, he/she is counted in the first study he/she participated in. If a subject/patient received both placebo or a comparator and celecoxib, he/she is counted only as a celecoxib subject/patient.
(b) See Table 1.1 for description of regimens.

Table 2.11
Summary of Uniquely Treated Subjects/Patients: All Trials

	Placebo	Celecoxib 5-50 mg	Celecoxib 100 mg	Celecoxib 200 mg QD	Celecoxib 200 mg	Celecoxib 300 mg	Celecoxib 400 mg	Celecoxib 600-1200 mg	Celecoxib + Other Drug	Active Control or Other Drug
ANALGESIA - SURGICAL PAIN(c)	100	0	113	0	104	0	0	0	0	104
COMBINED STUDIES	1954	1107	3419	930	3573	10	753	55	17	2255

Table A.47.1 Duration of Exposure to Cx (Phase 1, OA, RA, pain)

Table 3.3
Duration of Exposure: Phase I Trials (a)

	Placebo	Celecoxib 5-50 mg	Celecoxib 100 mg	Celecoxib 200 mg QD	Celecoxib 200 mg	Celecoxib 300 mg	Celecoxib 400 mg	Celecoxib 600-1200 mg	Celecoxib + Other Drug	Active Control or Other Drug
COMBINED STUDIES										
1 day	38	12	31	108	5	2	11	24	64	64
2-14 days	241	32	104	3	434	8	56	21	77	516
> 14 days	12	8	0	0	0	0	12	0	0	0
Number Treated	291	52	135	111	439	10	119	55	133	280

Note: 5 50 mg = 5, 10, 25, 40, or 50 mg. 600-1200 mg = 600, 800, 900, or 1200 mg.
(a) Days of exposure are added for patients who received the same dose in multiple periods.
See Table 3.2 for description of regimens.

Table 3.9
Duration of Exposure: OA Trials

	Placebo	Celecoxib 25-40 mg	Celecoxib 50 mg	Celecoxib 100 mg	Celecoxib 200 mg QD	Celecoxib 200 mg	Celecoxib 400 mg	Active Control
OA NORTH AMERICAN								
1-14 days	289	67	88	165	31	128	10	35
15-42 days	484	126	121	440	204	194	89	271
43-77 days	274	0	76	316	218	128	0	192
78-91 days	261	0	368	368	0	737	0	611
> 91 days	21	0	17	19	0	29	0	34
Number Treated	1329	193	490	1311	653	1208	99	1349
OA INTERNATIONAL (042):								
1-14 days				14				13
15-42 days				128				241
43-77 days				204				147
78-91 days				0				0
> 91 days				0				0
Number Treated				346				141
COMBINED OA								
1-14 days	289	67	88	179	31	128	10	111
15-42 days	484	126	121	568	204	194	89	512
43-77 days	274	0	76	520	218	128	0	339
78-91 days	261	0	368	368	0	737	0	611
> 91 days	21	0	17	19	0	29	0	34
Number Treated	1329	193	490	1657	653	1208	99	1725

Note: 25-40 mg = 25 or 40 mg
All Celecoxib regimens are BID unless otherwise specified.

Table 3.1
Duration of Exposure: RA Trials

	Placebo	Celecoxib 40 mg	Celecoxib 100 mg	Celecoxib 200 mg	Celecoxib 400 mg	Active Control
RA NORTH AMERICAN						
1-14 days	136	13	51	42	69	56
15-42 days	167	67	90	384	166	122
43-77 days	32	0	61	82	52	85
78-91 days	172	0	255	382	248	432
> 91 days	8	0	11	16	7	13
Number Treated	535	80	468	706	516	710
RA INTERNATIONAL (041):						
1-14 days				16		17
15-42 days				19		26
43-77 days				9		16
78-91 days				5		5
> 91 days				276		282
Number Treated				326		119
COMBINED RA						
1-14 days	136	13	51	58	69	73
15-42 days	167	67	90	293	166	148
43-77 days	32	0	61	91	52	101
78-91 days	172	0	255	388	248	437
> 91 days	8	0	11	282	7	295
Number Treated	535	80	468	1032	516	1156

Note: All celecoxib regimens are BID unless otherwise specified.