Table 2

Listing of End Points and Their Statistical Analyses

End Point	Statistical Analysis
Efficacy	
Pain Assessment at Each Time Point	
Pain Relief, PID, PRID, APAR, APID	ANOVA †, plot of mean with 84% CI over time.
TOPAR, SPID	ANOVA †, plot of mean with 84% CI over time.
Pain Intensity on Days 2 to 5	ANOVA†, Tukey trend test to compare rofecoxib doses with the placebo, plot of mean with 84% confidence interval over time
Overall Analgesic Effect	
TOPAR8, SPID8, patient's global evaluation at 8 and at 12 hours on Day 1	Analysis of Variance Model (ANOVA) †, plot of LSMean with 84% confidence interval (CI) at 8 hours for TOPAR8, plot and summary table of percent of patients in each category of the global evaluation score by treatment at 8 and 72 hours postdose.
Patient's Global Evaluation, Supplemental Rescue Medication, and Pain Intensity Averaged Over Days 2 to 5	ANOVA model†, plot of LSMean with 84% CI, plot
Percent of Patients Who Took Supplemental Rescue Medication Any of Days 2 to5	Logistic regression model†, bar chart of proportion of patients taking rescue medication for each treatment
Onset of Analgesic Effect	
Time to Confirmed Perceptible Pain Relief (Stopwatch Time to Perceptible Pain Relief, confirmed by the second stopwatch), Time to PID ³1	Cox proportional hazards regression model†, non-parametric log-rank test, Kaplan-Meier estimates of 25, 50, and 75th percentiles and 95% CI for the 50th percentile, plot of cumulative proportion of patients with meaningful Pain Relief or PID ³1 over time (1 Kaplan-Meier estimates of survival function), bar chart of incidence rates;
Duration of Analgesic Effect	
Time to Rescue Medication Use	Cox proportional hazards regression model ‡ and Kaplan-Meier estimates of 25, 50, and 75th percentiles and 95% CI for the 50% percentile, plot of cumulative proportion of patients requiring rescue medication over time (1-Kaplan Meier estimates of survival function).
Percent of Patients Who Took Rescue Medication during 0 to 12 hours post dose	Logistic regression model†, bar chart of proportion of patients taking rescue medication for each treatment
Pain Relief, PID, PRID at 12 hours	ANOVA †, plot of LSMean with 84% CI
Peak Analgesic Effect	
Peak PID and peak pain relief	ANOVA †, plot of LSMean with 84% CI

† Model included factors for sequence, patient nested within sequence, period within square, treatment, baseline Pain Intensity, and carryover (i.e., residual) effects. The carryover effect was removed from the model when it was determined not significant at 5% level.

‡ Model included factors for treatment and baseline Pain Intensity effects. The treatment-by-baseline Pain Intensity was tested and removed from the model if it was found not significant at 5% level.

End Point	Statistical Analysis
Safety	
Vital Signs and Laboratory Safety Parameters	
Percent of patients with predefined changes in vital signs and laboratory parameters	Cochran-Armitage trend test for the comparison between the rofecoxib 50-mg/50-mg group and the placebo group, and Fisher's exact test for the others. Results were interpreted using a step-down procedure.
Observed or log (observed value) for vital signs and laboratory parameters	Summary statistics, plot of observed mean and mean change from baseline with 84% confidence limits over time
Adverse Experience Counts	
Number (%) of patients with adverse experiences (including by category)	Cochran-Armitage trend test for the comparison between the rofecoxib dose groups and the placebo groups, and Fisher's exact test for the others. Results were interpreted using a step-down procedure

Comparisons With the Naproxen/Placebo Group on Days 2 to 5

Naproxen sodium was discontinued after the first dose on Day and patients who received naproxen sodium on Day 1 were switched to placebo on Days 2 to 5 and the reason given by the sponsor was a concern that the rofecoxib group would get a possible placebo response from the evening dose of medication.

RESULTS:

Disposition of Patients

Baseline demographic characteristics are presented in Table 3.
Of the 218 randomized patients, 57.8% were women, and 42.2% were men, 92.7% percent were white and 7.3% were of other origins. Patients' ages ranged from 32 to 87 years. The mean patient age was 64.7 years. Twenty-nine point eight percent of patients were older than 60 years of age; 29.4% of patients were older than 70 years of age; 6.9% of patients were older than 80 years of age. There were no clinically meaningful differences between the treatment groups for any of these characteristics.

Table 3
Baseline Patient Characteristics

	All Patients (N= 218)	
	n	(%)
Gender		
Female	126	(57.8)
Male	92	(42.2)
Race		
Asian	1	(0.5)
Black	12	(5.5)
European	1	(0.5)
Hispanic American	1	(0.5)
Indian	1	(0.5)
White	202	(92.7)
Age		
31 to 40	5	(2.3)
41 to 50	23	(10.6)
51 to 60	46	(21.1)
61 to 70	65	(29.8)
71 to 80	64	(29.4)
81 to 90	15	(6.9)
Mean	64.7	
SD	11.66	
Median	66.0	
Range	32 to 87	

Baseline Pain Intensity Score

The additional patient characteristics of surgery type, baseline pain intensity, primary route of administration of postoperative pain medication, duration of surgery, and number of hours from end of surgery to dosing of study medication are summarized in Table 4. There were no clinically meaningful differences between the treatment groups for any of these additional characteristics.

Table 4
Additional Patient Characteristics by Treatment Group

	Placebo/Placebo (N= 53)		Rofecoxib 50 mg/ 25 mg (N= 56)		Rofecoxib 50 mg/ 50 mg (N= 54)		Naproxen Sodium 550 mg/ Placebo (N= 55)		Total Patients (N= 218)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Type of Surgery										
Fracture Repair	2	(3.8)	0	(0.0)	0	(0.0)	2	(3.6)	4	(1.8)
Hip Surgery	21	(39.6)	27	(48.2)	25	(46.3)	25	(45.5)	98	(45.0)
Knee Surgery	30	(56.6)	29	(51.8)	29	(53.7)	28	(50.9)	116	(53.2)
Baseline Pain Intensity										
Moderate	43	(81.1)	45	(80.4)	44	(81.5)	46	(83.6)	178	(81.7)
Severe	10	(18.9)	11	(19.6)	10	(18.5)	9	(16.4)	40	(18.3)
Route of Administration of Postoperative Medications										
PCA †	31	(58.5)	32	(57.1)	34	(63.0)	34	(61.8)	131	(60.1)
Epidural †	19	(35.8)	20	(35.7)	15	(27.8)	15	(27.3)	69	(31.7)
PCA and epidural	0	(0.0)	0	(0.0)	2	(3.7)	0	(0.0)	2	(0.9)
Other ††	3	(5.7)	4	(7.1)	3	(5.6)	6	(10.9)	16	(7.3)
Number of Hours From End of Surgery to Dosing										
Mean	43.1		46.1		45.0		44.9		44.8	
Standard Deviation	12.8		14.9		11.1		16.2		13.9	
Median	45.1		46.6		45.4		46.0		45.6	
Range	15.4 to 70.9		17.3 to 96.8		20.6 to 71.4		16.3 to 93.3		15.4 to 96.8	

† PCA or Epidural patients may also have received intramuscular, intravenous injection, or oral postoperative pain medications (nonsteroidal anti-inflammatory agents, narcotics, and anesthetic agents).
†† Intramuscular, oral, or intravenous injection postoperative medications (NSAIDS, narcotics, and anesthetic agents).

Accounting for Patients in the Study

Of the 218 randomized patients, 175 (80.3%) completed the protocol as specified. The overall discontinuation rate was higher in the placebo/placebo group (Table 4). Because of the change in study treatment on Days 2 to 5, the patient accounting was separated by Day 1 versus Days 2 to 5 (Table 5 and Table 6). On Day 1, a significantly greater percentage of patients discontinued from the placebo group due to lack of efficacy compared to the rofecoxib or naproxen treatment groups (13.2, 3.6, and 1.8% respectively.)

Table 4
Patient Accounting

	Placebo/Placebo		Rofecoxib 50 mg/ 25 mg		Rofecoxib 50 mg/ 50 mg		Naproxen Sodium 550 mg/ Placebo		Total Patients	
ENTERED:	53		56		54		55		218	
Male (age range)	21 (32 to 85)		24 (36 to 80)		29 (44 to 82)		18 (42 to 84)		92 (32 to 85)	
Female (age range)	32 (41 to 83)		32 (40 to 81)		25 (40 to 84)		37 (38 to 87)		126 (38 to 87)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
COMPLETED:	35	(66.0)	45	(80.4)	46	(85.2)	49	(89.1)	175	(80.3)
DISCONTINUED:	18	(34.0)	11	(19.6)	8	(14.8)	6	(10.9)	43	(19.7)
Clinical adverse experience	8	(15.1)	3	(5.4)	4	(7.4)	3	(5.5)	18	(8.3)
Lack of efficacy	9	(17.0)	2	(3.6)	4	(7.4)	1	(1.8)	16	(7.3)
Patient withdrew consent	0	(0.0)	4	(7.1)	0	(0.0)	1	(1.8)	5	(2.3)
Protocol deviation	1	(1.9)	2	(3.6)	0	(0.0)	1	(1.8)	4	(1.8)

Table 5
Patient Accounting—Day 1

Study Status	Placebo N	(%)	MK- 0966 50 mg N	(%)	Naproxen 550 mg N	(%)	Total N	(%)
ENTERED †	53		110		55		218	
COMPLETED DAY 1:	42	(79.2%)	96	(87.3%)	51	(92.7%)	189	(86.7%)
DISCONTINUED— DAY 1:	11	(20.8%)	14	(12.7%)	4	(7.3%)	29	(13.3%)
Clinical adverse experience	3	(5.7%)	5	(4.6%)	2	(3.6%)	10	(4.6%)
Lack of efficacy	7	(13.2%)	4	(3.6%)*	1	(1.8%)*	12	(5.5%)
Patient withdrew consent	0	(0%)	4	(3.6%)	1	(1.8%)	5	(2.3%)
Protocol deviation	1	(1.9%)	1	(0.9%)	0	(0%)	2	(1.7%)

* $p \leq 0.050$ versus placebo.

Table 6
Patient Accounting—Days 2 to 5

	Placebo/Placebo		Rofecoxib 50 mg/ 25 mg		Rofecoxib 50 mg/ 50 mg		Naproxen Sodium 550 mg/ Placebo		Total Patients	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
CONTINUED PAST DAY 1	42		48		48		51		189	
COMPLETED DAYS 2 TO 5 :	35	(83.3%)	45	(93.8%)	46	(95.8%)	49	(96.1%)	175	(92.6%)
DISCONTINUED— DAYS 2 TO 5:	7	(16.7%)	3	(6.3%)	2	(4.2%)*	2	(3.9%)	14	(7.4%)
Clinical adverse experience	5	(11.9%)	1	(2.1%)*	1	(2.1%)*	1	(2.0%)	8	(4.2%)
Lack of efficacy	2	(4.8%)	1	(2.1%)	1	(2.1%)	0	(0%)	4	(2.1%)
Patient withdrew consent	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Protocol deviation	0	(0%)	1	(2.1%)	0	(0%)	1	(2.0%)	2	(2.6%)

Accounting for Patients in the Analysis

All patients who took study medication recorded a baseline pain intensity score of moderate or severe and recorded at least one pain evaluation postdose on Day 1. Therefore, all patients were included in the efficacy analysis.

Analysis of Primary Efficacy Measures

Pain Intensity score, Pain Relief score, Patient's Global Evaluation, and Time to Rescue Medication were all recorded. The sponsor chose Total of Pain Relief Scores Over 8 Hours (TOPAR8), Sum of Pain Intensity Differences Over 8 Hours (SPID8), Patient's Global Evaluation Score at 8 Hours, and Total Dose of Supplemental Rescue Medication as the measures for overall analgesic effect.
The reviewer preferred the Division's approach and analyzed first the time specific Mean Pain Intensity Difference Scores (PID) and the Mean Pain Relief Scores (PR) as primary measures of analgesic efficacy.

Mean Pain Intensity Difference Scores Over Time (PID, LOCF and BOCF)

Figure 2 and table 7 present the mean PID scores at all assessment times during the first 12 hour Treatment Period. The PID scores were calculated by subtracting the pain intensity at a specific assessment time from the baseline pain intensity. Imputing pain intensity data has been done using last observation carried forward (LOCF) method.

The mean PID values for the rofecoxib 50 mg treatment group were statistically significantly better than placebo at all assessment times from the 1 hour through 12 hours postdose.

The mean PID scores for the Naproxen Na 550 mg group were statistically significant better than placebo from 1 hour through 12 hours postdose. The mean PID scores for the Naproxen Na 550 mg group were not statistically different than those for the rofecoxib 50 mg group at any time.

Reanalyzing the data by using the baseline observation carried forward (BOCF) technique revealed the same results except at 6 and 7 hours where the Naproxen Na 550 mg group did not separate from placebo.

Figure 2

Mean Pain Intensity Difference (PID) Score With
84% Confidence Interval by Hours Postdose
(Intention-to-Treat Approach)

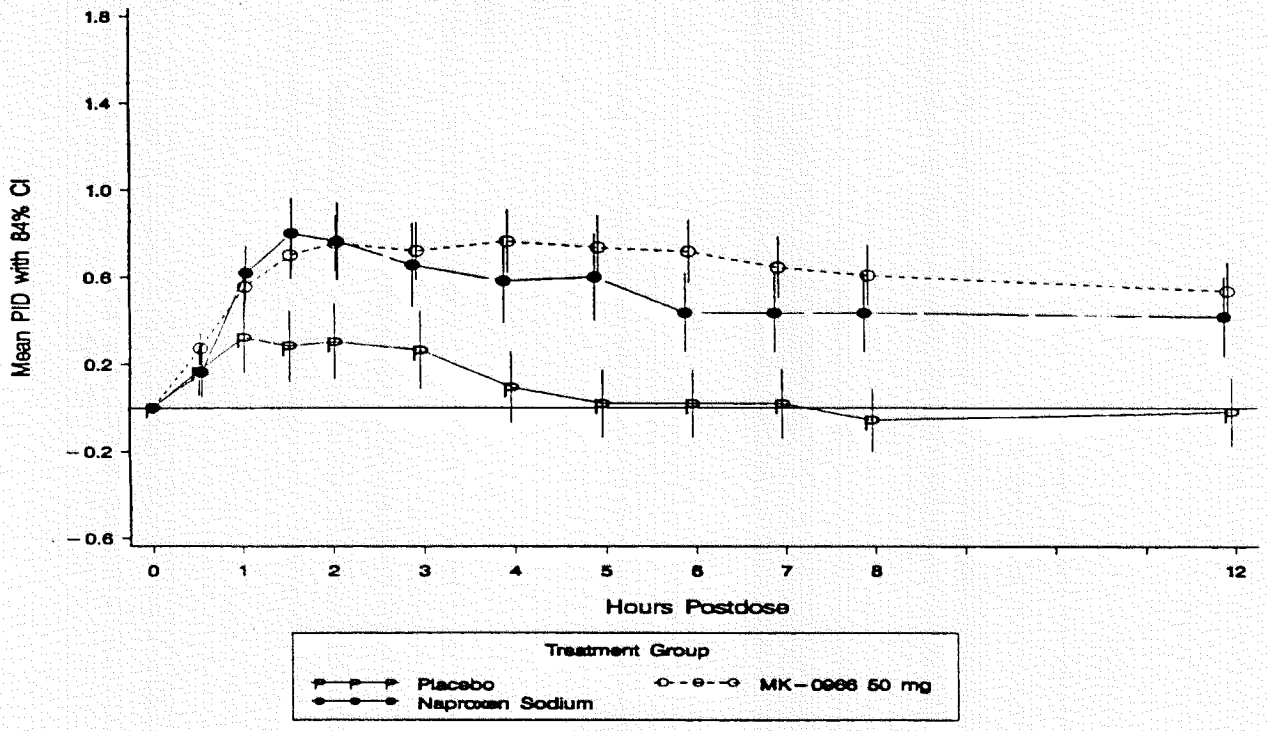


Table 11
Analysis of Pain Intensity Difference by Time Point (Intention-to-Treat Approach)

Treatment		Summary Statistics by Time Point (Hours Postdose)										
		0.5	1	1.5	2	3	4	5	6	7	8	12
Placebo	N	53	53	45	33	27	21	16	8	8	7	2
	MEAN	0.2A†	0.3B	0.3B	0.3B	0.2B	0.1B	0.0B	0.0B	0.0B	-0.1B	-0.0B
	STD	0.6	0.8	0.9	0.9	0.9	0.9	0.80.8	0.8	0.8	0.8	0.8
Rofecoxib 50 mg	N	110	110	97	86	80	68	58	53	46	46	40
	MEAN	0.3A	0.6A	0.7A	0.8A	0.7A	0.8A	0.7A	0.7A	0.6A	0.6A	0.5A
	STD	0.6	0.7	0.8	0.9	0.9	1.1	1.1	1.1	1.1	1.0	1.0
Naproxen Na 550 mg	N	55	55	52	49	44	32	28	27	21	19	14
	MEAN	0.2A	0.6A	0.8A	0.8A	0.7A	0.6A	0.6A	0.4A	0.4A	0.4A	0.4A
	STD	0.6	0.7	0.8	0.9	0.9	1.0	1.0	1.0	1.0	0.9	0.9
†A, B, C — Letter A indicates the most effective dose(s), B indicates the next most effective, and so forth.												
p- Values From Between- Treatment Pairwise Comparisons by Time Point (Hours Postdose)												
Pairwise Comparison		0.5	1	1.5	2	3	4	5	6	7	8	12
Rofecoxib 50 mg vs. Placebo		0.379	0.038	0.003	0.003	0.005	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Naproxen Na 550 mg vs. Placebo		0.833	0.017	<0.001	0.006	0.020	0.006	0.002	0.019	0.018	0.005	0.010
Naproxen Na 550 mg vs. 50 mg		0.256	0.493	0.339	0.809	0.899	0.400	0.565	0.120	0.264	0.346	0.590

Mean Pain Relief Scores Over Time (PR, LOCF and BOCF)

Figure 3 and table 8 present the mean PR scores at all assessment times during the first 12 hour Treatment Period. Imputing pain relief data has been done using last observation carried forward (LOCF) method.

The mean PR values for the rofecoxib 50 mg treatment group were statistically significantly better than placebo at 1 hour through 12 hours postdose.

The mean PR scores for the Naproxen Na 550 mg group were statistically significant better than placebo from 1 hour through 12 hours postdose. The mean PR scores for the Naproxen Na 550 mg group were not statistically different than those for the rofecoxib 50 mg group at any time through 12 hours postdose.

Reanalyzing the data by using the baseline observation carried forward (BOCF) technique revealed the same results.

Mean Pain Intensity Difference and Pain Relief (PRID, LOCF and BOCF)

Table 9 and figure 4 present the mean PRID scores at all assessment times during the first 12 hour Treatment Period. Imputing pain intensity data has been done using last observation carried forward (LOCF) method.

The mean PRID values for the rofecoxib 50 mg treatment group were statistically significantly better than placebo at all assessment times from the 1 hours through 12 hours postdose.

The mean PRID scores for the Naproxen Na 550 mg group were statistically significant better than placebo from 1 hour through 12 hours postdose. The mean PRID scores for the Naproxen Na 550 mg group were not statistically different than those for the rofecoxib 50 mg group at any time.

Reanalyzing the data by using the baseline observation carried forward (BOCF) technique revealed the same results.

Figure 4
Mean PRID Scores by Hour Postdose

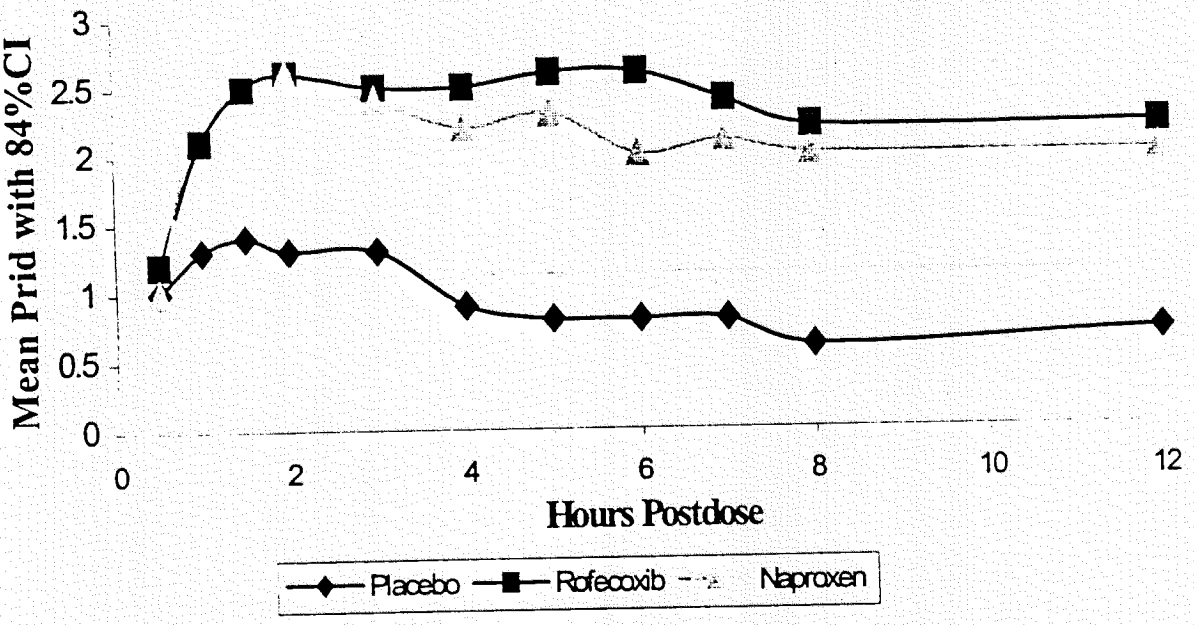


Table 9
Analysis of PRID by Time Point (Intention-to-Treat Approach)

Treatment		Summary Statistics by Time Point (Hours Postdose)										
		0.5	1	1.5	2	3	4	5	6	7	8	12
Placebo	N	53	53	45	33	27	21	16	8	8	7	2
	MEAN	1.0A†	1.3	1.4	1.3	1.3	0.9	0.8	0.8	0.8	0.6	0.7
	STD	1.5	1.9	2.1	2.0	2.0	1.7	1.8	1.6	1.8	1.5	1.7
Rofecoxib 50 mg	N	110	110	97	86	80	68	58	53	46	46	40
	MEAN	1.2A	2.1	2.5	2.6	2.5	2.5	2.6	2.6	2.4	2.2	2.2
	STD	1.4	1.7	1.9	2.3	2.3	2.6	2.6	2.6	2.5	2.5	2.4
Naproxen Na 550 mg	N	55	55	52	49	44	32	28	27	21	19	14
	MEAN	1.0	2.4	2.7	2.6	2.4	2.2	2.3	2.0	2.1	2.0	2.0
	STD	1.5	1.6	1.9	2.1	2.3	2.4	2.5	2.3	2.3	2.3	2.3
†A, B, C — Letter A indicates the most effective dose(s), B indicates the next most effective, and so forth.												
p- Values From Between- Treatment Pairwise Comparisons by Time Point (Hours Postdose)												
Pairwise Comparison		0.5	1	1.5	2	3	4	5	6	7	8	12
Rofecoxib 50 mg vs. Placebo		0.695	0.011	0.002	<0.001	0.002	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Naproxen Na 550 mg vs. Placebo		0.756	0.001	<0.001	0.002	0.014	0.004	0.002	0.005	0.005	0.001	0.001
Naproxen Na 550 mg vs. 50 mg		0.448	0.206	0.345	0.819	0.819	0.476	0.562	0.162	0.42	0.386	0.783

Total of Pain Relief Scores to 8 Hours (TOPAR8)

Figure 3 shows a plot of the mean Pain Relief score versus hours postdose. The TOPAR8, was an estimate of the area under the Pain Relief versus time curve during the first 8 hours postdose.

The least-squares mean (LSMean) TOPAR8 scores in patients who received placebo, rofecoxib 50 mg, or naproxen sodium 550 mg were 5.8, 12.3, and 11.7 units, respectively (Table 10).

Over the 8 hours postdose, rofecoxib 50 mg had significantly ($p<0.001$) greater TOPAR8 value compared with placebo. (Table 10).

The LSMean TOPAR8 score for naproxen sodium 550 mg was significantly ($p=0.002$) greater than that for placebo, but not significantly different from the LSMean score for rofecoxib 50 mg (Table 10).

Table 10
Analysis of Total Pain Relief Score Over 8 Hours (TOPAR8)
(Intention-to-Treat Approach)

Treatment	N	Mean	SD	LSMean	95% CI for LSMean
Placebo	53	7.1	8.1	5.8	(2.9, 8.7)
MK- 0966 50 mg	110	13.9	10.6	12.3	(10.2, 14.5)
Naproxen Sodium	55	13.0	9.9	11.7	(8.8, 14.5)

Pairwise Comparison	Difference in LSMeans	95% CI for Difference	p- Value
MK- 0966 50 mg vs. Placebo	6.5	(3.4, 9.7)	<0.001
Naproxen Sodium vs. Placebo	5.8	(2.2, 9.5)	0.002
Naproxen Sodium vs. 50 mg	-0.7	(- 3.8, 2.4)	0.665

Effect	p- Value	Pooled Intra- Patient SD
Treatment	<0.001	9.6
Center (Study Site)	0.045	
Surgical Procedure (Surgery)	0.144	
Baseline Pain Intensity (PI)	0.035	
Treatment- by- Baseline PI Interaction	0.905	
Treatment- by- Center Interaction	0.700	
Treatment- by- Surgery Interaction	0.323	

Sum of Pain Intensity Difference to 8 Hours (SPID8)

Figure 2 shows the mean PID score plotted versus hours postdose. The SPID8 was an estimate of the area under the PID versus time curve during the 8 hours postdose.

The LSMean SPID8 scores in patients who received placebo, rofecoxib 50 mg, and naproxen sodium 550 mg were 1.8, 6.2, and 5.5 units, respectively (Table11).

Over the 8 hours postdose, rofecoxib 50 mg had significantly ($p<0.001$) greater SPID8 score compared with placebo (Table 11).

The LSMean SPID8 score for naproxen sodium 550 mg was significantly ($p=0.004$) greater than that for placebo but not significantly different from the score in rofecoxib 50 mg. (Table 11).

Table 11
Analysis of Sum of Pain Intensity Difference to 8 Hours (SPID8)
(Intention-to-Treat Approach)

Treatment	N	Mean	SD	LSMean	95% CI for LSMean
Placebo	53	0.8	5.9	1.8	(- 0.1, 3.8)
MK- 0966 50/ 25 mg	110	5.3	7.1	6.2	(4.8, 7.6)
Naproxen Sodium	55	4.3	6.4	5.5	(3.6, 7.3)

Pairwise Comparison	Difference in LSMeans	95% CI for Difference	p- Value
MK- 0966 50/ 25 mg vs. Placebo	4.4	(2.3, 6.5)	<0.001
Naproxen Sodium vs. Placebo	3.6	(1.2, 6.0)	0.004
Naproxen Sodium vs. 50/ 25 mg	-0.7	(- 2.8, 1.3)	0.479

Effect	p- Value	Pooled Intra- Patient SD
Treatment	<0.001	6.4
Center (Study Site)	0.054	
Surgical Procedure (Surgery)	0.035	
Baseline Pain Intensity (PI)	0.005	
Treatment- by- Baseline PI Interaction	0.753	
Treatment- by- Center Interaction	0.581	
Treatment- by- Surgery Interaction	0.246	

Patient's Global Evaluation at 8 Hours

The LSMean scores for placebo, rofecoxib 50 mg, and naproxen sodium 550 mg were 1.0, 1.8, and 1.7, respectively (Table 12).

Compared with placebo, the 50-mg dose of rofecoxib was associated significantly (p=0.002) greater LSMean Patient Global Evaluation score at 8 hours (Table 12).

Patient's Global Evaluation score at 8 hours for naproxen sodium 550 mg was significantly (p=0.009) greater than that for placebo. The difference between naproxen sodium 550 mg and rofecoxib 50 mg was not significant. (Table 12).

Table 12
Analysis of Sum of Patient's Global Evaluation at 8 Hours
(Intention-to-Treat Approach)

Treatment	N	Mean	SD	LSMean	95% CI for LSMean
Placebo	50	1.2	1.3	1.0	(0.6, 1.5)
MK- 0966 50/ 25 mg	102	2.0	1.5	1.8	(1.5, 2.1)
Naproxen Sodium	51	2.0	1.3	1.7	(1.3, 2.2)

Pairwise Comparison	Difference in LSMeans	95% CI for Difference	p- Value
MK- 0966 50/ 25 mg vs. Placebo	0.8	(0.3, 1.3)	0.002
Naproxen Sodium vs. Placebo	0.7	(0.2, 1.3)	0.009
Naproxen Sodium vs. 50/ 25 mg	0.0	(- 0.5, 0.4)	0.878

Effect	p- Value	Pooled Intra- Patient SD
Treatment	0.005	1.4
Center (Study Site)	0.244	
Surgical Procedure (Surgery)	0.243	
Baseline Pain Intensity (PI)	0.072	
Treatment- by- Baseline PI Interaction	0.482	
Treatment- by- Center Interaction	0.943	
Treatment- by- Surgery Interaction	0.648	

Peak Analgesic Effect During 8 Hours Postdose

The LSMean Peak PID scores during 8 hours for placebo, rofecoxib 50 mg, and naproxen sodium 550 mg were 0.8, 1.3, and 1.2, respectively (Figure 5). The LSMean Peak Pain Relief scores during 8 hours for placebo, rofecoxib 50 mg, and naproxen sodium 550 mg were 1.5, 2.2, and 2.3, respectively (Figure 5&6).

During the 8 hours postdose, rofecoxib 50 mg demonstrated a significantly greater ($p<0.001$) Peak PID and ($p=0.002$) Peak Pain Relief compared with placebo.

The Peak PID and Peak Pain Relief scores for naproxen sodium 550 mg were significantly ($p=0.005$) greater than placebo. The Peak PID and Peak Pain Relief scores for naproxen sodium 550 mg were not significantly different from rofecoxib 50 mg.

Figure 5

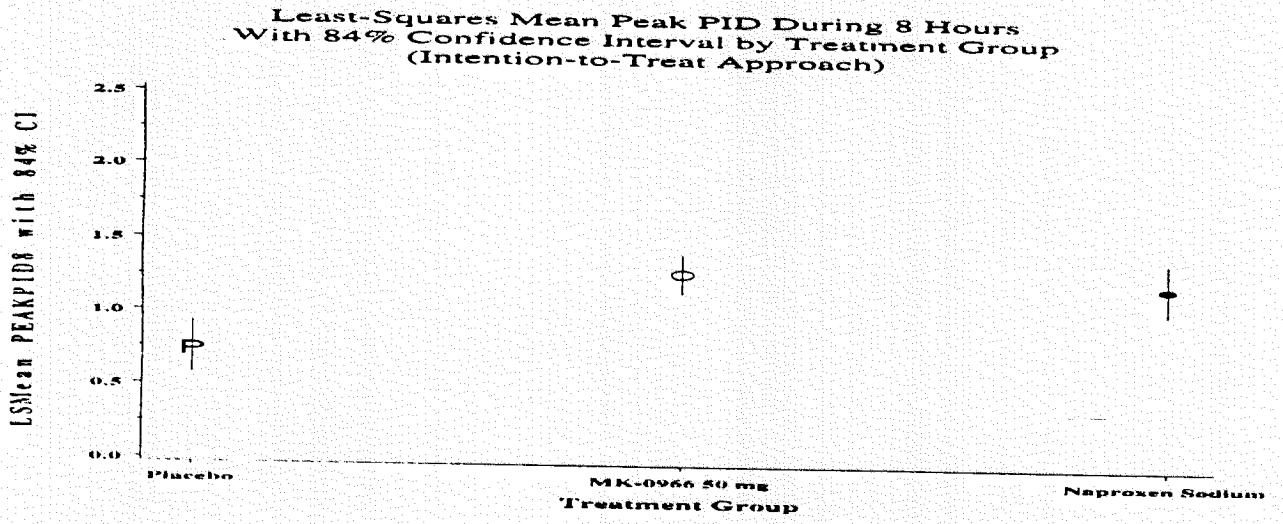
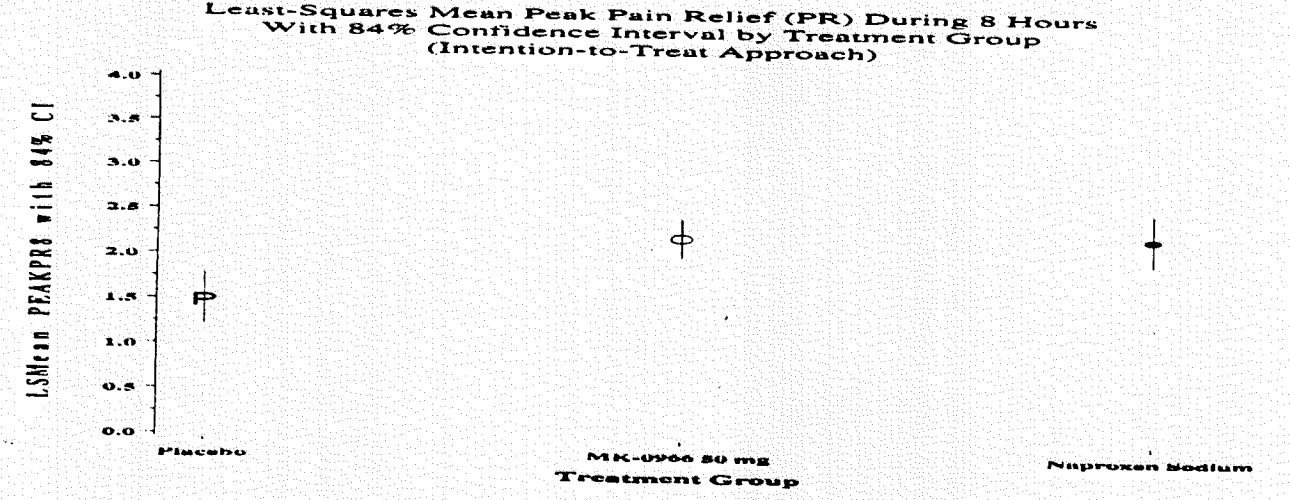


Figure 6



Onset of Analgesic Effect on Day 1 - Time to Confirmed Perceptible Pain Relief Within 4 Hours Postdose (Stopwatch Time of Perceptible Pain Relief, Confirmed by the Second Stopwatch)

There were 39.6, 58.2, and 52.7% of patients who experienced Confirmed Perceptible Pain Relief in the placebo, rofecoxib 50-mg, and naproxen sodium 550-mg groups, respectively. The median Times to Confirmed Perceptible Pain Relief (estimated time when 50% of patients experienced Confirmed Perceptible Pain Relief) for patients in the rofecoxib 50 mg and naproxen sodium 550-mg groups were 0.9 and 1.2 hours, respectively. The median time for the placebo group could not be uniquely estimated because approximately 60% of the patients did not experience Confirmed Perceptible Pain Relief within the 4-hour evaluation period specified in the protocol.

Comparison of the cumulative incidence curves indicated that the time to Confirmed Perceptible Pain Relief was significantly ($p=0.017$) shorter in patients who received rofecoxib 50 mg compared with those who received placebo.

The time to Confirmed Perceptible Pain Relief for the 550-mg naproxen sodium group was numerically shorter and approached statistical significance ($p=0.074$) compared with the time for the placebo group. The difference in the time to Confirmed Perceptible Pain Relief was not significant between the 50-mg rofecoxib and 550-mg naproxen sodium groups ($p=0.405$).

Duration of Analgesic Effect

1) Time to Rescue Medication

Patients in the active-treatment groups who underwent hip replacement required rescue medication later than those in the same groups who underwent knee replacement or fracture repair. Conversely, patients in the placebo group who underwent hip replacement required rescue medication earlier than those who underwent knee replacement or fracture repair. In the combined group, the median Times to Rescue Medication (the time when 50% patients took rescue medication) for patients in the placebo, rofecoxib 50-mg, and naproxen sodium 550-mg groups were 2.8, 5.3, and 5.3 hours, respectively (Table 13).

The median time to rescue medication in the group that received rofecoxib 50-mg was significantly longer ($p<0.001$) than that in the group that received placebo.

Patients who received naproxen sodium 550-mg were associated with a significantly longer median time to rescue medication compared with those who received placebo ($p=0.004$). The median Time to Rescue Medication in the rofecoxib 50-mg and naproxen sodium 550-mg groups were similar (Table 13).