Summary ID#4091

Clinical Study Summary: Study F1J-MC-HMAT Study Group B

Title of Study: Duloxetine Versus Placebo and Paroxetine in the Acute Treatment of Major Depression	
Investigator(s): This multicenter study included 20 principal investigators.	
Study Center(s): There were 22 study sites (two investigators had satellite sites) in the United States.	
Length of Study: 11 months Date first patient enrolled: 09 March 2000 Date last patient completed: 06 February 2001	**Phase of Development:** 3

Objectives: The primary objective of this study was to demonstrate that duloxetine 40 mg twice daily (BID) is superior to placebo in the acute treatment of patients with *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV)–defined major depressive disorder (MDD).

The secondary objectives of this study were:

- To compare the safety of duloxetine 20 mg BID, duloxetine 40 mg BID, placebo, and paroxetine using information on discontinuation rates, treatment-emergent adverse events (TEAEs), discontinuation-emergent adverse events, laboratory analyses, vital signs, and electrocardiograms (ECGs).
- To compare the efficacy of duloxetine 40 mg BID with paroxetine as measured by a noninferiority test of mean 17-item Hamilton Depression Rating Scale ($HAMD_{17}$) total scores at Visit 8. Data from each of the two studies (HMAT Study Group A and Study Group B) will be combined for this comparison.
- To assess the efficacy of duloxetine 20 mg BID and duloxetine 40 mg BID compared with placebo as measured by response and remission rates.
- To compare the time to onset of action (defined as time to meeting responder criteria) of duloxetine 20 mg BID, duloxetine 40 mg BID, and paroxetine.
- To compare the efficacy of duloxetine 20 mg BID, duloxetine 40 mg BID, placebo, and paroxetine on anxiety symptoms associated with depression as measured by mean endpoint scores on the Hamilton Anxiety Rating Scale (HAMA) and the anxiety subscale of the $HAMD_{17}$.
- To compare the efficacy of duloxetine 20 mg BID, duloxetine 40 mg BID, placebo, and paroxetine as measured by mean endpoint scores (after adjusting for baseline differences) on the Clinical Global Impressions of Severity scale (CGI-Severity), the Montgomery and Asberg Depression Rating Scale (MADRS), $HAMD_{17}$ subfactor scores, and endpoint scores on the Patient's Global Impressions of Improvement scale (PGI-Improvement).
- To compare the efficacy of duloxetine 20 mg BID, duloxetine 40 mg BID, placebo, and paroxetine on somatic complaints of pain using the Somatic Symptom Inventory scale (SSI) and Visual Analog Scales (VAS).
- To compare the impact of treatment with duloxetine 20 mg BID, duloxetine 40 mg BID, placebo, and paroxetine on sexual functioning as measured by the Arizona Sexual Experiences Scale (ASEX).
- To compare the impact of treatment with duloxetine 20 mg BID, duloxetine 40 mg BID, placebo, and paroxetine on quality of life as measured by the Quality of Life in Depression Scale (QLDS), and on medical resource utilization and work productivity as measured by the Resource Utilization scale.

Study Design: Multicenter, parallel, double-blind, randomized, placebo- and active comparator-controlled study with blinded placebo lead-in and placebo lead-out. The protocol consisted of two identical studies conducted in parallel and reported separately (Study Group A and Study Group B). The study consisted of two study periods.

Study Period I was the 1-week screening phase of the study, and Study Period II was an 11-week acute therapy phase in which patients were assessed weekly from Visit 2 (Week 0) to Visit 5 (Week 3) and every other week from Visit 5 (Week 3) to Visit 9 (Week 11). This study design employed double-blind, variable-duration placebo lead-in and lead-out periods to blind patients and investigators at the start and end of active therapy. Figure HMATb.1 illustrates the study design.

Number of Patients:
Planned: 356 patients (89 per treatment group)
Randomized: 86 Duloxetine 20 mg BID; 91 Duloxetine 40 mg BID ; 89 Placebo; 87 Paroxetine 20 mg QD.
Completed: 55 Duloxetine 20 mg BID; 53 Duloxetine 40 mg BID; 52 Placebo; 49 Paroxetine 20 mg QD.

Diagnosis and Main Criteria for Inclusion: Male and female outpatients of at least 18 years of age with a primary diagnosis of MDD as defined by the DSM-IV, and confirmed by use of the Mini International Neuropsychiatric Interview (MINI). Patients were required to have a $HAMD_{17}$ total score ≥15 and a CGI-Severity total score ≥4 at both Visit 1 and Visit 2.

Test Product, Dose, and Mode of Administration: Duloxetine capsules, 20 mg; patients took 40 mg orally twice daily or 20 mg orally twice daily.

Duration of Treatment:
Duloxetine: 8 weeks
Paroxetine: 8 weeks
Placebo: 11 weeks

Reference Therapy, Dose, and Mode of Administration:
Paroxetine 20 mg capsules; patients took 20 mg orally once daily.
Placebo capsules

Variables:
Efficacy: The primary efficacy measure was the $HAMD_{17}$ total score. Secondary efficacy measures included $HAMD_{17}$ response rates (50% reduction from baseline to endpoint), $HAMD_{17}$ remission rates (endpoint score ≤7), time to sustained response, and time to sustained remission. Other secondary measures included the $HAMD_{17}$ subfactors and individual items, MADRS, CGI-Severity, PGI-Improvement, HAMA, Somatic Symptom Inventory (SSI) 26- and 28-item scale, and Visual Analog Scales (VAS) for pain.

Safety: Safety was evaluated through the collection and reporting of discontinuation rates, TEAEs, discontinuation-emergent adverse events, laboratory analyses, vital signs, ECGs, and the ASEX.

Health Outcomes: Health outcomes were evaluated using the QLDS scale and Health Resource Utilization scales. Health Resource Utilization results will not be reported in this synopsis.

Evaluation Methods:

Statistical:

The primary efficacy comparison was between duloxetine 40 mg BID and placebo, based on the likelihood-based repeated measures analysis. The terms in the repeated measure analysis model included treatment, visit, investigative site, baseline score, and the interactions of visit with treatment and baseline score. For secondary measures, an analysis of covariance (ANCOVA)/analysis of variance (ANOVA) model containing terms for treatment, investigator, and baseline score (no baseline score term in ANOVA model) was used for continuous variables. Categorical variables such as response and remission rates were evaluated using Fisher's exact test and the Cochran-Mantel-Haenszel (CMH) chi-square test with investigative site as strata. Time to event data, such as time to onset of action, were analyzed using the Kaplan-Meier method, and the treatment group differences were tested by the log-rank and Wilcoxon tests.

An intent-to-treat (ITT) principle was applied in all efficacy and safety analyses. For all total scores calculated from individual items, if any of the individual items was missing, the corresponding total score was considered missing. Sites with fewer than 8 randomly assigned patients with baseline and at least one postbaseline (Visit 4 to Visit 8) $HAMD_{17}$ total score were pooled. If this resulted in a pooled site with fewer than 8 patients, these patients were pooled with the next smallest site. For efficacy and safety analyses, treatment group differences were tested at a 2-sided significance level of 0.05.

The planned sample size (356 patients) provides 83% power to detect a difference between the duloxetine 40 mg BID and placebo groups of 3.25 points in mean change from baseline to endpoint of the $HAMD_{17}$ total score, assuming a common standard deviation of 7.0, 90% of patients would provide at least one baseline and one postbaseline assessment, and using a two-sided test with α=0.05. Using data pooled from Study Group A and Study Group B, this sample size also provides 80% power to test the non-inferiority of duloxetine 40 mg BID compared with paroxetine using a one-sided 97.5% confidence interval and an equivalence limit of –2.2 for mean $HAMD_{17}$ scores.

Summary:

Disposition/Demographics (Table HMATb.1): A total of 353 patients were randomly assigned and enrolled into the study. Of these, 209 patients completed the acute therapy phase (placebo, n=52; duloxetine 20 mg BID, n=55; duloxetine 40 mg BID, n=53; paroxetine 20 mg QD, n=49) and 206 completed the entire study. The percentages of patients who discontinued for any reason during the acute therapy phase were similar among the four treatment groups. No statistically significant differences were observed among treatment groups with regard to age, gender, origin, or height. Patients had a mean age of approximately 40 years, with the majority being Caucasian and female.

Efficacy Measures (Tables HMATb.2, Table HMATb.3)**:** Patients treated with duloxetine at both doses (20 mg BID and 40 mg BID) had statistically significantly greater improvement in the primary efficacy measure ($HAMD_{17}$ total score) compared with placebo-treated patients, by repeated measures analysis. Paroxetine-treated patients did not differ statistically significantly from the placebo group on this measure. Mean change analyses revealed the same results. Patients treated with duloxetine 40 mg BID showed statistically significantly greater improvement in scores on the primary efficacy measure ($HAMD_{17}$ total score) compared with paroxetine-treated patients at endpoint.

Patients treated with duloxetine 40 mg BID met the criteria for treatment response and remission at endpoint statistically significantly more frequently than did patients treated with placebo. Patients treated with either duloxetine 40 mg BID or paroxetine had statistically significantly shorter time to first response than did patients treated with placebo.

Patients treated with duloxetine 40 mg BID showed statistically significantly greater improvement on the $HAMD_{17}$ subfactor scores of Anxiety/Somatization, Core Factor, Maier, and Retardation as compared with placebo-treated patients.

Patients treated with duloxetine 40 mg BID showed statistically significantly greater improvement on the MADRS total score compared with placebo-treated patients, by repeated measures analysis. Mean change analysis revealed the same result. Duloxetine 20 mg BID, paroxetine- and placebo-treated patients did not differ statistically significantly on this measure.

Patients treated with duloxetine 40 mg BID showed statistically significantly greater improvement on the HAMA scale compared with placebo-treated patients (despite the fact that this trial excluded patients with primary anxiety disorders). Mean change analyses revealed the same result. Paroxetine- and placebo-treated patients did not differ statistically significantly on this measure.

Patients treated with duloxetine 40 mg BID showed statistically significantly greater improvement on the Visual Analog Scale (VAS) for overall pain severity compared with placebo-treated patients, and showed marginally statistically significantly greater improvement on the VAS for amount of time in pain while awake. Mean change analyses revealed the same results.

Patients treated with duloxetine 40 mg BID showed statistically significantly greater improvement on the Quality of Life in Depression Scale (QLDS), and showed a statistically significantly greater percentage of patients with reductions in the types of health care providers visited and the number of visits to health care providers, compared with placebo-treated patients.

There were statistically significantly fewer discontinuations due to perceived lack of efficacy for patients treated with both doses of duloxetine compared with placebo-treated patients.

Using 2.2 as the noninferiority margin, it is shown that duloxetine 40 mg BID treatment was noninferior to paroxetine treatment using either repeated measure analysis or mean change analysis. In addition, even when using a more stringent noninferiority margin than 2.2 (namely, using one-half of the absolute gain of paroxetine over placebo), it remains true that duloxetine 40 mg BID treatment was noninferior to paroxetine treatment using repeated measures analysis.

Safety — Acute Therapy Phase:

Deaths/Serious Adverse Events/Discontinuations Due to Adverse Events: No patients died during this study. Two patients experienced serious adverse events postrandomization. One patient receiving duloxetine 40 mg BID had an accidental injury falling from a horse, suffering a concussion and a subsequent seizure. One patient receiving paroxetine relapsed into alcohol abuse, suffered alcohol withdrawal symptoms, and was admitted for detoxification. In the acute therapy phase 40 (11.3%) of 353 discontinued due to an adverse event. There were no statistically significant differences among treatment groups with respect to adverse events reported as a reason for discontinuation in the acute therapy phase. The percentages of patients who discontinued for any reason were similar among the four treatment groups.

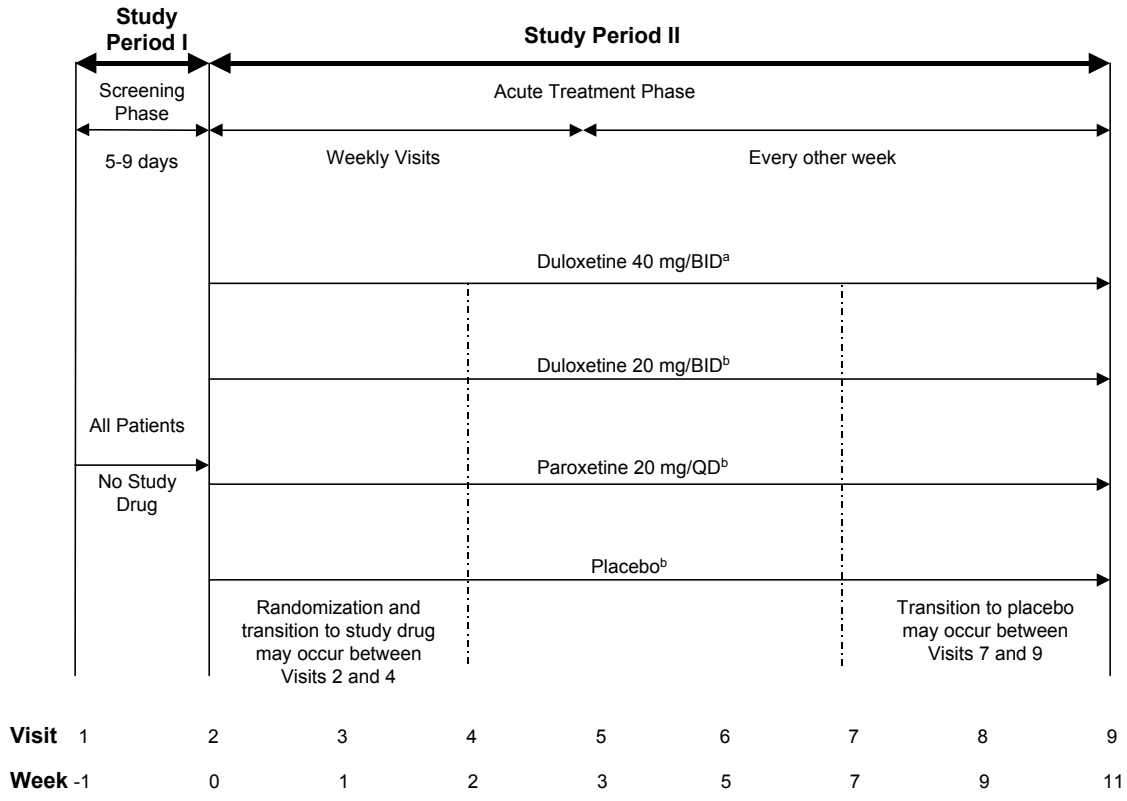

Figure HMAT.1. Illustration of study design for Protocol F1J-MC-HMAT.

Table HMATb.1. Patient Characteristics at Baseline
All Randomized Patients

Variable	PLACEBO (N=89)	DLX20BID (N=86)	DLX40BID (N=91)	PRX20QD (N=87)	Total (N=353)	p-Value
AGE: YRS						
No. Patients	89	86	91	87	353	.949**
Mean	40.14	40.69	40.89	40.25	40.50	
Median	41.28	40.05	40.83	39.25	40.29	
Standard Dev.	12.94	10.04	11.90	11.02	11.50	
Minimum	20.07	20.56	18.20	19.18	18.20	
Maximum	78.21	70.60	68.87	64.02	78.21	
HEIGHT: CM (Visit: 1)						
No. Patients	89	85	91	87	352	.556**
Mean	170.84	170.66	169.45	169.19	170.03	
Median	170.18	167.64	167.64	170.18	167.64	
Standard Dev.	9.69	9.66	10.72	9.79	9.97	
Minimum	152.40	152.40	139.70	149.86	139.70	
Maximum	198.12	200.66	195.58	193.04	200.66	
Unspecified	0	1	0	0	1	
WEIGHT: KG (Visit: 1)						
No. Patients	88	86	90	87	351	.071**
Mean	80.22	81.61	82.19	88.75	83.18	
Median	77.86	78.09	81.95	79.00	79.00	
Standard Dev.	18.93	20.33	20.87	28.97	22.74	
Minimum	45.40	51.76	43.58	45.40	43.58	
Maximum	153.91	165.26	155.72	194.31	194.31	
Unspecified	1	0	1	0	2	

Table HMATb.1. Patient Characteristics at Baseline
All Randomized Patients (concluded)

Variable	PLACEBO (N=89)	DLX20BID (N=86)	DLX40BID (N=91)	PRX20QD (N=87)	Total (N=353)	p-Value
ORIGIN: NO. (%)						
No. Patients	89	86	91	87	353	.270*
African Descent	8 (9.0)	4 (4.7)	5 (5.5)	9 (10.3)	26 (7.4)	
Western Asian	0	0	0	2 (2.3)	2 (0.6)	
Caucasian	74 (83.1)	72 (83.7)	77 (84.6)	64 (73.6)	287 (81.3)	
East/Southeast A	1 (1.1)	0	0	0	1 (0.3)	
Hispanic	6 (6.7)	9 (10.5)	9 (9.9)	12 (13.8)	36 (10.2)	
Other	0	1 (1.2)	0	0	1 (0.3)	
GENDER: NO. (%)						
No. Patients	89	86	91	87	353	.633*
Female	57 (64.0)	48 (55.8)	56 (61.5)	56 (64.4)	217 (61.5)	
Male	32 (36.0)	38 (44.2)	35 (38.5)	31 (35.6)	136 (38.5)	

Output stored as RMP.F1JO.HMAT.FINALB(DE128006)
Data from RMP.SAS.F1JM.MCHMATSW.STUDYB
* Frequencies are analyzed using a Chi-Square test.
** Means are analyzed using a Type III Sum of Squares analysis of variance (ANOVA): PROC GLM model=investigator and treatment.
XDES0001

Table HMATb.2. Summary of Efficacy and Health Outcome Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb

	Treatment Group				p-Value		
Variable	**Placebo**	**Dulox 20 BID**	**Dulox 40 BID**	**Parox 20 QD**	**Dulox 20 vs placebo**	**Dulox 40 vs placebo**	**Parox 20 vs placebo**
$HAMD_{17}$ Total Score	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	17.19 (5.11)	18.63 (5.85)	18.06 (4.52)	17.65 (5.13)			
Mean Change (SD)	–4.16 (6.42)	–7.17 (7.97)	–7.72 (7.67)	–6.06 (8.12)	p=.022	p=.003	p=.150
LS Mean Change (SE)	–4.99 (0.81)	–7.42 (0.80)	–8.61 (0.81)[a]	–6.22 (0.82)	p=.034	p=.002	p=.285
$HAMD_{17}$ Response Rate	n=88	n=84	n=86	n=84			
Responders n (%)	27 (31%)	37 (44%)	44 (51%)	34 (40%)	.083	.009	.204
$HAMD_{17}$ Remission Rate	n=88	n=84	n=86	n=84			
Remitters n (%)	26 (30%)	29 (35%)	43 (50%)	31 (37%)	.516	.008	.334
$HAMD_{17}$ Subscale – Core	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	7.43 (2.64)	8.05 (2.53)	7.36 (2.14)	7.65 (2.43)			
Mean Change (SD)	–2.02 (3.39)	–3.37 (3.53)	–3.40 (3.14)	–3.00 (3.87)	p=.023	p=.008	p=.110
LS Mean Change (SE)	–2.64 (0.39)	–3.66 (0.38)	–4.00 (0.39)	–3.24 (0.39)	p=.060	p=.013	p=.271
$HAMD_{17}$ Subscale – Maier	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	9.26 (3.00)	9.88 (3.01)	9.47 (2.28)	9.33 (2.64)			
Mean Change (SD)	–2.53 (3.56)	–4.04 (4.25)	–4.30 (3.90)	–3.75 (4.33)	p=.028	p=.004	p=.057
LS Mean Change (SE)	–3.06 (0.44)	–4.18 (0.43)	–4.79 (0.44)	–4.03 (0.44)	p=.068	p=.005	p=.115

Table HMATb.2. Summary of Efficacy and Health Outcome Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb (continued)

	Treatment Group				p-Value		
Variable	**Placebo**	**Dulox 20 BID**	**Dulox 40 BID**	**Parox 20 QD**	**Dulox 20 vs placebo**	**Dulox 40 vs placebo**	**Parox 20 vs placebo**
$HAMD_{17}$ Subscale – Anxiety/Somatization	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	5.48 (2.12)	6.04 (2.52)	6.07 (1.82)	5.85 (2.41)			
Mean Change (SD)	–1.06 (2.49)	–2.17 (3.08)	–2.79 (2.72)	–2.13 (3.23)	p=.046	p=<.001	p=.040
LS Mean Change (SE)	–1.38 (0.29)	–2.11 (0.28)	–2.92 (0.28)[a]	–2.11 (0.29)	p=.066	p=<.001	p=.069
$HAMD_{17}$ Subscale – Retardation/Somatization	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	6.38 (1.97)	6.96 (2.11)	6.34 (1.75)	6.81 (1.95)			
Mean Change (SD)	–1.80 (2.84)	–2.80 (3.03)	–2.63 (2.80)	–2.45 (3.15)	p=.047	p=.053	p=.263
LS Mean Change (SE)	–2.32 (0.32)	–3.08 (0.32)	–3.22 (0.32)	–2.59 (0.33)	p=.092	p=.046	p=.546
$HAMD_{17}$ Subscale – Sleep	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	2.67 (1.87)	2.76 (1.86)	2.85 (1.82)	2.54 (1.85)			
Mean Change (SD)	–0.81 (1.91)	–1.05 (2.04)	–1.02 (2.29)	–0.69 (2.16)	p=.485	p=.769	p=.827
LS Mean Change (SE)	–0.84 (0.21)	–1.04 (0.20)	–1.14 (0.21)	–0.65 (0.21)	p=.483	p=.303	p=.503

Table HMATb.2. Summary of Efficacy and Health Outcome Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb (continued)

	Treatment Group				p-Value		
Variable	**Placebo**	**Dulox 20 BID**	**Dulox 40 BID**	**Parox 20 QD**	**Dulox 20 vs placebo**	**Dulox 40 vs placebo**	**Parox 20 vs placebo**
$HAMD_{17}$ Item #1 Score	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	2.32 (0.89)	2.52 (0.80)	2.24 (0.77)	2.37 (0.79)			
Mean Change (SD)	–0.67 (1.24)	–1.08 (1.19)	–0.95 (1.02)	–0.96 (1.31)	p=.054	p=.065	p=.122
LS Mean Change (SE)	–0.89 (0.13)	–1.15 (0.13)	–1.16 (0.13)	–1.11 (0.13)	p=.174	p=.152	p=.255
MADRS	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	22.72 (8.00)	24.44 (8.05)	22.58 (6.21)	23.07 (7.51)			
Mean Change (SD)	–5.75 (9.19)	–9.11 (11.50)	–8.99 (10.08)	–8.51 (11.91)	p=.082	p=.029	p=.105
LS Mean Change (SE)	–7.43 (1.15)	–9.37 (1.14)	–10.73 (1.16)	–9.01 (1.17)	p=.227	p=.042	p=.331
CGI-Severity	n=88	n=84	n=87	n=85			
Mean Baseline (SD)	4.11 (0.73)	4.19 (0.80)	4.10 (0.51)	4.02 (0.62)			
Mean Change (SD)	–0.88 (1.21)	–1.19 (1.38)	–1.20 (1.26)	–1.06 (1.39)	p=.135	p=.078	p=.262
LS Mean Change (SE)	–1.10 (0.15)	–1.36 (0.15)	–1.42 (0.16)	–1.25 (0.16)	p=.242	p=.153	p=.507

Table HMATb.2. Summary of Efficacy and Health Outcome Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb (concluded)

	Treatment Group				p-Value		
Variable	Placebo	Dulox 20 BID	Dulox 40 BID	Parox 20 QD	Dulox 20 vs placebo	Dulox 40 vs placebo	Parox 20 vs placebo
PGI-Improvement	n=88	n=84	n=86	n=85			
Mean Baseline (SD)	n/a	n/a	n/a	n/a			
Endpoint Mean (SD)	3.24 (1.41)	2.93 (1.31)	2.86 (1.47)	2.99 (1.44)	p=.162	p=.079	p=.253
Endpoint LS Mean (SE)	2.87 (0.15)	2.74 (0.15)	2.52 (0.15)	2.80 (0.15)	p=.522	p=.093	p=.743
HAMA	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	14.48 (5.33)	15.25 (5.86)	14.88 (4.87)	14.49 (5.76)			
Mean Change (SD)	–3.49 (5.32)	–5.13 (6.74)	–5.86 (7.14)	–4.60 (7.36)	p=.149	p=.019	p=.257
LS Mean Change (SE)	–4.33 (0.69)	–5.45 (0.68)	–6.57 (0.69)	–5.23 (0.69)	p=.238	p=.020	p=.349
QLDS	n=80	n=76	n=78	n=72			
Mean Baseline (SD)	15.21 (7.32)	19.92 (7.37)	17.22 (7.67)	17.60 (8.49)			
Mean Change (SD)	–4.30 (8.21)	–9.29 (8.61)	–8.55 (9.39)	–7.96 (10.26)	p=.069	p=.023	p=.084
LS Mean Change (SE)	–7.87 (1.07)	–8.90 (1.04)	–10.76 (1.05)	–9.85 (1.04)	p=.483	p=.050	p=.178

Abbreviations: CGI-Severity = Clinical Global Impressions of Severity; HAMA = Hamilton Anxiety Rating Scale; $HAMD_{17}$ = 17-Item Hamilton Depression Rating Scale; MADRS = Montgomery and Asberg Depression Rating Scale; PGI-Improvement = Patient's Global Impressions of Improvement; Dulox 20 BID = duloxetine 20 mg twice daily; Dulox 40 BID = duloxetine 40 mg twice daily; Parox 20 QD = paroxetine 20 mg once daily; QLDS = Quality of Life in Depression Scale; SD = standard deviation; SE = standard error.

Note: n = the number of patients who had a baseline score and at least one nonmissing postbaseline score for that particular variable

Note: "n/a" in Global Impressions of Improvement scales indicates that a baseline score is not collected in this type of scale

Note: Mean Change – Data from mean change analysis

Note: LS Mean Change – Data from repeated measures analysis

[a] Result was statistically significant ($p \leq .05$) compared with paroxetine 20 mg QD

Table HMATb.3. Summary of Somatic and Pain Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb

	Treatment Group				p-Value		
Variable	**Placebo**	**Dulox 20 BID**	**Dulox 40 BID**	**Parox 20 QD**	**Dulox 20 vs placebo**	**Dulox 40 vs placebo**	**Parox 20 vs placebo**
SSI 26-Item Average	n=88	n=82	n=86	n=85			
Mean Baseline (SD)	1.68 (0.55)	1.71 (0.51)	1.71 (0.55)	1.71 (0.47)			
Mean Change (SD)	–0.13 (0.47)	–0.13 (0.35)	–0.17 (0.46)	–0.17 (0.47)	p=.700	p=.875	p=.732
LS Mean Change (SE)	–0.18 (0.05)	–0.15 (0.05)	–0.22 (0.05)	–0.22 (0.05)	p=.620	p=.621	p=.540
SSI 28-Item Average	n=88	n=82	n=86	n=85			
Mean Baseline (SD)	1.69 (0.56)	1.72 (0.51)	1.74 (0.57)	1.72 (0.49)			
Mean Change (SD)	–0.13 (0.47)	–0.13 (0.35)	–0.19 (0.46)	–0.17 (0.47)	p=.703	p=.640	p=.740
LS Mean Change (SE)	–0.18 (0.05)	–0.15 (0.05)	–0.24 (0.05)	–0.22 (0.05)	p=.636	p=.409	p=.581
VAS-Severity of Overall Pain	n=88	n=84	n=86	n=85			
Mean Baseline (SD)	24.18 (25.99)	27.02 (25.39)	25.55 (22.83)	22.22 (22.48)			
Mean Change (SD)	–3.20 (27.17)	–6.44 (23.30)	–10.34 (22.52)	–8.06 (20.26)	p=.710	p=.048	p=.071
LS Mean Change (SE)	–4.09 (2.49)	–5.08 (2.42)	–11.44 (2.49)	–9.63 (2.51)	p=.771	p=.035	p=.113

Table HMATb.3. Summary of Somatic and Pain Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb (continued)

	Treatment Group				p-Value		
Variable	**Placebo**	**Dulox 20 BID**	**Dulox 40 BID**	**Parox 20 QD**	**Dulox 20 vs placebo**	**Dulox 40 vs placebo**	**Parox 20 vs placebo**
VAS-Severity of Headaches	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	23.68 (28.58)	20.63 (23.70)	22.42 (23.30)	16.05 (20.63)			
Mean Change (SD)	–6.17 (25.39)	–3.36 (22.70)	–7.99 (24.03)	–3.40 (23.08)	p=.677	p=.470	p=.603
LS Mean Change (SE)	–6.25 (2.30)	–5.56 (2.23)	–7.90 (2.30)	–6.83 (2.32)	p=.828	p=.607	p=.859
VAS-Severity of Back Pain	n=88	n=84	n=86	n=85			
Mean Baseline (SD)	17.23 (22.76)	22.31 (26.11)	20.19 (24.61)	15.87 (18.07)			
Mean Change (SD)	–1.19 (25.30)	–6.88 (21.83)	–8.31 (24.05)	–3.36 (20.01)	p=.414	p=.094	p=.387
LS Mean Change (SE)	–2.48 (2.41)	–5.06 (2.35)	–7.67 (2.41)	–4.19 (2.43)	p=.439	p=.124	p=.612
VAS-Severity of Shoulder Pain	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	14.64 (23.56)	12.65 (19.58)	15.98 (22.24)	13.68 (22.73)			
Mean Change (SD)	–2.40 (20.09)	–2.07 (19.53)	–7.97 (21.61)	–2.71 (22.95)	p=.899	p=.081	p=.907
LS Mean Change (SE)	–2.34 (2.26)	–2.98 (2.19)	–5.67 (2.26)	–0.82 (2.26)	p=.837	p=.292	p=.631

Table HMATb.3. Summary of Somatic and Pain Measures
Mean Change from Baseline to Endpoint/Last Observation
All Randomized Patients
Acute Therapy Phase F1J-MC-HMATb (concluded)

	Treatment Group				p-Value		
Variable	**Placebo**	**Dulox 20 BID**	**Dulox 40 BID**	**Parox 20 QD**	**Dulox 20 vs placebo**	**Dulox 40 vs placebo**	**Parox 20 vs placebo**
VAS-Interference with Daily Activities	n=88	n=84	n=86	n=85			
Mean Baseline (SD)	17.14 (25.42)	19.52 (24.66)	17.00 (21.00)	15.62 (20.91)			
Mean Change (SD)	–3.38 (26.49)	–1.94 (26.44)	–4.90 (25.39)	–3.29 (20.77)	p=.261	p=.687	p=.915
LS Mean Change (SE)	–4.31 (2.53)	–0.57 (2.45)	–6.79 (2.52)	–4.24 (2.53)	p=.281	p=.482	p=.983
VAS-Pain While Awake	n=88	n=84	n=86	n=84			
Mean Baseline (SD)	25.73 (28.05)	34.93 (32.52)	29.23 (27.28)	28.30 (30.51)			
Mean Change (SD)	–1.95 (30.33)	–8.18 (31.49)	–10.99 (32.23)	–8.10 (32.52)	p=.787	p=.078	p=.269
LS Mean Change (SE)	–2.43 (3.32)	–2.70 (3.23)	–11.36 (3.31)	–6.02 (3.33)	p=.952	p=.055	p=.440

Abbreviations: Dulox 20 BID = duloxetine 20 mg twice daily; Dulox 40 BID = duloxetine 40 mg twice daily; Parox 20 QD = paroxetine 20 mg once daily; SSI = Somatic Symptom Inventory; VAS = Visual Analog Scales

Note: n = the number of patients who had a baseline score and at least one nonmissing postbaseline score for that particular variable

Note: Mean Change – Data from mean change analysis

Note: LS Mean Change – Data from repeated measures analysis

Table HMATb.4. Treatment-Emergent Adverse Events with Incidence Greater than or Equal to 2 Percent
All Randomized Patients
Acute Therapy Phase

	PLACEBO N=89 n(%)	DLX20BID N=86 n(%)	DLX40BID N=91 n(%)	PRX20QD N=87 n(%)	Total N=353 n(%)	p-Values* Overall	1vs2	1vs3	1vs4	2vs3	2vs4	3vs4
PATIENTS WITH >= 1 TESS	61(68.5)	73(84.9)	76(83.5)	76(87.4)	286(81.0)	.009	.013	.023	.003	.839	.666	.528
NAUSEA	2(2.2)	19(22.1)	23(25.3)	14(16.1)	58(16.4)	<.001	<.001	<.001	.001	.724	.339	.143
HEADACHE	10(11.2)	12(14.0)	17(18.7)	10(11.5)	49(13.9)	.470	.652	.211	1.00	.423	.655	.213
INSOMNIA	5(5.6)	15(17.4)	18(19.8)	7(8.0)	45(12.7)	.008	.017	.006	.564	.705	.072	.031
RHINITIS	15(16.9)	7(8.1)	5(5.5)	7(8.0)	34(9.6)	.075	.110	.018	.110	.558	1.00	.560
SOMNOLENCE	2(2.2)	15(17.4)	10(11.0)	7(8.0)	34(9.6)	.005	<.001	.033	.098	.281	.072	.613
DIZZINESS	5(5.6)	4(4.7)	15(16.5)	9(10.3)	33(9.3)	.032	1.00	.031	.278	.014	.248	.276
DRY MOUTH	3(3.4)	9(10.5)	14(15.4)	7(8.0)	33(9.3)	.042	.077	.009	.209	.377	.611	.165
DIARRHEA	7(7.9)	7(8.1)	8(8.8)	10(11.5)	32(9.1)	.851	1.00	1.00	.454	1.00	.611	.624
CONSTIPATION	3(3.4)	7(8.1)	8(8.8)	12(13.8)	30(8.5)	.095	.207	.212	.015	1.00	.331	.346
PAIN	10(11.2)	6(7.0)	3(3.3)	6(6.9)	25(7.1)	.230	.434	.047	.433	.319	1.00	.322
SWEATING	0(0.0)	8(9.3)	11(12.1)	6(6.9)	25(7.1)	.003	.003	<.001	.013	.631	.590	.310
ASTHENIA	2(2.2)	8(9.3)	9(9.9)	4(4.6)	23(6.5)	.102	.055	.058	.441	1.00	.248	.250
DYSPEPSIA	6(6.7)	3(3.5)	6(6.6)	6(6.9)	21(5.9)	.743	.497	1.00	1.00	.498	.496	1.00
BACK PAIN	6(6.7)	7(8.1)	3(3.3)	3(3.4)	19(5.4)	.408	.779	.327	.497	.202	.211	1.00
ANOREXIA	1(1.1)	4(4.7)	10(11.0)	3(3.4)	18(5.1)	.028	.205	.009	.365	.164	.720	.082
VASODILATATION	2(2.2)	7(8.1)	6(6.6)	2(2.3)	17(4.8)	.158	.096	.278	1.00	.778	.099	.279
ABDOMINAL PAIN	2(2.2)	6(7.0)	4(4.4)	3(3.4)	15(4.2)	.457	.164	.682	.680	.527	.329	1.00
COUGH INCREASED	5(5.6)	3(3.5)	3(3.3)	4(4.6)	15(4.2)	.886	.720	.494	1.00	1.00	1.00	.716
LIBIDO DECREASED	1(1.1)	4(4.7)	7(7.7)	3(3.4)	15(4.2)	.163	.205	.064	.365	.537	.720	.331
VOMITING	1(1.1)	6(7.0)	5(5.5)	3(3.4)	15(4.2)	.203	.061	.211	.365	.762	.329	.721
MYALGIA	4(4.5)	4(4.7)	3(3.3)	3(3.4)	14(4.0)	.933	1.00	.719	1.00	.714	.720	1.00
NERVOUSNESS	2(2.2)	4(4.7)	5(5.5)	1(1.1)	12(3.4)	.355	.438	.444	1.00	1.00	.211	.211
AMBLYOPIA	1(1.1)	1(1.2)	6(6.6)	3(3.4)	11(3.1)	.159	1.00	.118	.365	.119	.621	.497
ANORGASMIA	0(0.0)	4(4.7)	4(4.4)	3(3.4)	11(3.1)	.174	.056	.121	.119	1.00	.720	1.00
ANXIETY	0(0.0)	4(4.7)	3(3.3)	4(4.6)	11(3.1)	.172	.056	.246	.058	.714	1.00	.716
PARESTHESIA	4(4.5)	1(1.2)	2(2.2)	4(4.6)	11(3.1)	.485	.368	.441	1.00	1.00	.368	.436
ACCIDENTAL INJURY	0(0.0)	5(5.8)	2(2.2)	3(3.4)	10(2.8)	.091	.027	.497	.119	.268	.496	.677
PHARYNGITIS	5(5.6)	2(2.3)	1(1.1)	2(2.3)	10(2.8)	.380	.444	.116	.444	.612	1.00	.615
ABNORMAL DREAMS	0(0.0)	2(2.3)	2(2.2)	5(5.7)	9(2.5)	.119	.240	.497	.028	1.00	.443	.270

(1) = PLACEBO, (2) = DLX20BID, (3) = DLX40BID, (4) = PRX20QD
*p-Values are from Fisher's Exact test.

Table HMATb.4. Treatment-Emergent Adverse Events with Incidence Greater than or Equal to 2 Percent
All Randomized Patients
Acute Therapy Phase (concluded)

	PLACEBO N=89 n(%)	DLX20BID N=86 n(%)	DLX40BID N=91 n(%)	PRX20QD N=87 n(%)	Total N=353 n(%)	p-Values* Overall	1vs2	1vs3	1vs4	2vs3	2vs4	3vs4
ABNORMAL EJACULATION	1(1.1)	2(2.3)	2(2.2)	4(4.6)	9(2.5)	.539	.616	1.00	.208	1.00	.682	.436
IMPOTENCE	0(0.0)	4(4.7)	2(2.2)	3(3.4)	9(2.5)	.165	.056	.497	.119	.434	.720	.677
TREMOR	1(1.1)	3(3.5)	2(2.2)	3(3.4)	9(2.5)	.682	.362	1.00	.365	.675	1.00	.677
FLATULENCE	1(1.1)	2(2.3)	1(1.1)	4(4.6)	8(2.3)	.424	.616	1.00	.208	.612	.682	.203
PALPITATION	2(2.2)	2(2.3)	2(2.2)	2(2.3)	8(2.3)	1.000	1.00	1.00	1.00	1.00	1.00	1.00
RASH	3(3.4)	1(1.2)	4(4.4)	0(0.0)	8(2.3)	.195	.621	1.00	.246	.369	.497	.121
TINNITUS	1(1.1)	4(4.7)	2(2.2)	1(1.1)	8(2.3)	.436	.205	1.00	1.00	.434	.211	1.00
NECK PAIN	0(0.0)	4(4.7)	3(3.3)	0(0.0)	7(2.0)	.031	.056	.246		.714	.059	.246
PRURITUS	2(2.2)	2(2.3)	1(1.1)	2(2.3)	7(2.0)	.881	1.00	.619	1.00	.612	1.00	.615
THINKING ABNORMAL	0(0.0)	1(1.2)	5(5.5)	1(1.1)	7(2.0)	.067	.491	.059	.494	.212	1.00	.211
TWITCHING	1(1.1)	3(3.5)	2(2.2)	1(1.1)	7(2.0)	.630	.362	1.00	1.00	.675	.368	1.00
URINARY FREQUENCY	0(0.0)	3(3.5)	2(2.2)	2(2.3)	7(2.0)	.398	.117	.497	.243	.675	.682	1.00

Table HMATb.5. Laboratory Data - Chemistry Analytes
Analytes with Statistically Significant Mean Change From Baseline to Endpoint Values
All Randomized Patients
Acute Therapy Phase

				Baseline		Change to Endpoint		p-Values	
Lab Test	Lab Unit	Therapy	n	Mean	SD	Mean	SD	Therapy (Int*1)	Pair-wse*2
AST	U/L	PLACEBO	86	24.29	10.86	-2.05	10.11	.008	
		DLX20BID	81	22.68	7.44	3.17	10.60	(.475)	.001
		DLX40BID	81	22.67	10.21	1.25	8.03		.010
		PRX20QD	78	23.54	10.55	1.47	10.88		.015
ALT	U/L	PLACEBO	86	27.73	20.40	-3.56	13.73	.002	
		DLX20BID	81	25.48	15.69	4.15	18.93	(.480)	.004
		DLX40BID	81	24.37	17.50	3.86	13.69		<.001
		PRX20QD	78	28.51	20.92	-0.53	15.77		.070
CPK	U/L	PLACEBO	86	192.0	673.6	-55.6	427.5	.013	
		DLX20BID	81	126.6	89.0	30.9	115.1	(.813)	.040
		DLX40BID	81	123.8	101.5	-6.7	129.3		.599
		PRX20QD	78	111.0	63.8	31.8	173.0		.039
ALKPH	U/L	PLACEBO	86	68.6	20.4	-1.4	9.1	.049	
		DLX20BID	81	69.7	19.5	3.9	12.8	(.585)	.013
		DLX40BID	81	70.1	18.2	2.4	9.2		.019
		PRX20QD	78	72.5	23.4	0.9	14.0		.153
CALC	mmol/L	PLACEBO	86	2.397	0.111	-0.035	0.126	.009	
		DLX20BID	81	2.379	0.112	-0.006	0.148	(.280)	.273
		DLX40BID	81	2.398	0.120	-0.003	0.144		.193
		PRX20QD	78	2.357	0.102	0.032	0.110		<.001
SODIUM	mmol/L	PLACEBO	86	141.7	2.1	-1.2	2.8	.020	
		DLX20BID	81	141.5	2.2	-0.4	2.9	(.554)	.079
		DLX40BID	81	141.5	2.7	-0.2	3.3		.014
		PRX20QD	78	141.2	2.4	0.2	3.0		.004
UR AC	umol/L	PLACEBO	86	288.8	87.8	1.0	43.6	.145	
		DLX20BID	81	314.4	82.8	-1.0	48.8	(.810)	.262
		DLX40BID	81	304.9	84.1	-17.1	47.8		.022
		PRX20QD	78	300.8	81.5	-5.5	48.3		.150
T.BILI	umol/L	PLACEBO	86	6.8	6.0	0.9	2.9	.016	
		DLX20BID	81	6.7	4.2	-0.0	3.6	(.808)	.017
		DLX40BID	81	7.1	5.6	-0.5	3.4		.008
		PRX20QD	78	6.2	3.7	0.6	2.9		.591

Output stored as RMP.F1JO.HMAT.FINALB(LS604002)
Data from RMP.SAS.F1JM.MCHMATSW.STUDYB
Note: n = Total number of patients in each treatment group having the variable in both baseline and postbaseline visits.

Note: Models:

RDUC1 - *1 Type III Sums of Squares from an analysis of variance (ANOVA) on the ranks: PROC GLM model=investigator and treatment for the overall p-Value and model=investigator, treatment, and interaction for the interaction p-Value.
*2 Least-squares mean option in PROC GLM from the ANOVA on the ranks using the mean square for error.
Note: Each investigator has at least one patient in each treatment group.

Table HMATb.5. Laboratory Data - Chemistry Analytes
Analytes with Statistically Significant Mean Change From Baseline to Endpoint Values
All Randomized Patients
Acute Therapy Phase

Legend of Lab Test Code Abbreviations:

Abbrev.	Description
AST	AST/SGOT
ALT	ALT/SGPT
CPK	CREATINE PHOSPHOKINASE
ALKPH	ALKALINE PHOSPHATASE
CALC	CALCIUM
SODIUM	SODIUM
UR AC	URIC ACID
T.BILI	BILIRUBIN, TOTAL

Table HMATb.6. Laboratory Data - Nonchemistry Analytes
Analytes with Statistically Significant Mean Change From Baseline to Endpoint Values
All Randomized Patients
Acute Therapy Phase

				Baseline		Change to Endpoint		p-Values		
Lab Test	Lab Unit	Therapy	n	Mean	SD	Mean	SD	Therapy (Int*1)	Pair-wse*2	Model
HCT	1	PLACEBO	79	0.4189	0.0394	-0.0090	0.0278	.067		RDUC1
		DLX20BID	76	0.4237	0.0364	0.0011	0.0240	(.613)	.019	
		DLX40BID	76	0.4233	0.0350	-0.0007	0.0259		.067	
		PRX20QD	67	0.4201	0.0398	-0.0057	0.0263		.634	
MCHC	mml/L-Fe	PLACEBO	79	21.0	1.1	0.1	1.1	.225		RDUC1
		DLX20BID	76	21.0	0.8	-0.2	1.0	(.736)	.047	
		DLX40BID	76	21.0	1.0	0.0	1.1		.583	
		PRX20QD	67	21.0	1.0	0.0	1.2		.628	
WBC	GI/L	PLACEBO	80	7.43	1.76	-0.31	1.21	.043		RDUC1
		DLX20BID	76	7.24	1.83	0.18	1.76	(.053)	.085	
		DLX40BID	77	7.85	2.23	-0.44	1.64		.359	
		PRX20QD	69	7.60	1.99	0.08	1.92		.245	
BANDS	GI/L	PLACEBO	80	0.000	0.000	0.000	0.000	*		FULL3
		DLX20BID	76	0.000	0.000	0.000	0.000	(*)	*	
		DLX40BID	77	0.000	0.000	0.000	0.000		*	
		PRX20QD	69	0.000	0.000	0.000	0.000		*	
POLYS	GI/L	PLACEBO	80	4.565	1.391	-0.284	1.084	.074		RDUC1
		DLX20BID	76	4.514	1.411	0.140	1.604	(.345)	.143	
		DLX40BID	77	4.942	1.731	-0.340	1.498		.511	
		PRX20QD	69	4.709	1.590	0.144	1.679		.126	
BASO	GI/L	PLACEBO	80	0.046	0.027	0.004	0.037	.034		RDUC1
		DLX20BID	76	0.049	0.027	0.003	0.025	(.420)	.400	
		DLX40BID	77	0.051	0.029	0.007	0.028		.178	
		PRX20QD	69	0.055	0.031	-0.005	0.045		.140	
MCV	fL	PLACEBO	79	89.0	5.4	-0.9	4.1	.055		RDUC1
		DLX20BID	76	89.6	5.1	0.9	3.8	(.879)	.006	
		DLX40BID	76	89.3	4.9	0.1	3.9		.226	
		PRX20QD	67	89.7	4.5	0.0	4.7		.157	
U-SPGR	NO UNITS	PLACEBO	54	1.0194	0.0082	-0.0007	0.0080	.013		RDUC2
		DLX20BID	52	1.0175	0.0075	0.0012	0.0087	(.335)	.212	
		DLX40BID	51	1.0177	0.0073	0.0039	0.0071		.001	
		PRX20QD	47	1.0197	0.0077	0.0021	0.0088		.060	
TSH	mU/L	PRX20QD	2	0.835	0.021	0.165	0.148			
CK-MB	ng/ml	PLACEBO	1	17.30		-4.20				
CKMBRI	ngL/Uml	PLACEBO	1	0.30		0.20				

Table HMATb.6. Laboratory Data - Nonchemistry Analytes
Analytes with Statistically Significant Mean Change From Baseline to Endpoint Values
All Randomized Patients
Acute Therapy Phase (concluded)

Note: n = Total number of patients in each treatment group having the variable in both baseline and postbaseline visits.

Note: Models:

FULL3 - *1 Type III Sums of Squares from an analysis of variance (ANOVA) on the ranks: PROC GLM model=inv., treatment, and interaction.
*2 Least-squares mean option in PROC GLM from the ANOVA on the ranks using the mean square for error.
Note: Each investigator has at least one patient in each treatment group.

RDUC1 - *1 Type III Sums of Squares from an analysis of variance (ANOVA) on the ranks: PROC GLM model=investigator and treatment for the overall p-Value and model=investigator, treatment, and interaction for the interaction p-Value.
*2 Least-squares mean option in PROC GLM from the ANOVA on the ranks using the mean square for error.
Note: Each investigator has at least one patient in each treatment group.

RDUC2 - *1 Type III Sums of Squares from an analysis of variance (ANOVA) on the ranks: PROC GLM model=investigator and treatment for the overall p-Value and model=investigator, treatment, and interaction for the interaction p-Value.
*2 Least-squares mean option in PROC GLM from the ANOVA on the ranks using the mean square for error.
Note: At least one investigator does not have patients in every treatment group.

*Note: Error sum of squares is equal to 0, thus no p-Values are computed.

Legend of Lab Test Code Abbreviations:

Abbrev.	Description
HCT	HEMATOCRIT
MCHC	MEAN CELL HEMOGLOBIN CONCENTRATION (MCHC)
WBC	LEUKOCYTE COUNT
BANDS	BANDS
POLYS	NEUTROPHILS, SEGMENTED
BASO	BASOPHILS
MCV	MEAN CELL VOLUME (MCV)
U-SPGR	UA-SPECIFIC GRAVITY
TSH	THYROID STIM. HORMONE
CK-MB	CK-MB (IMX)
CKMBRI	CK-MB RELATIVE INDEX

Table HMATb.7. Summary of Vital Signs and Weight Change from Baseline to Endpoint All Randomized Patients Acute Therapy Phase

	Treatment Group			
Variable	Placebo	Dulox 20	Dulox 40	Paroxetine
Heart rate (bpm)	n=86	n=84	n=87	n=85
Mean baseline (SD)	73.50 (8.40)	71.75 (11.04)	71.02 (8.10)	71.20 (9.75)
Mean change (SD)	-1.66 (8.47)	0.75 (10.02)	2.02 (9.86)	-0.21 (10.03)
p-value (active vs placebo)		.172	.044	.524
Systolic blood pressure (mmHg)	n=86	n=84	n=87	n=85
Mean baseline (SD)	119.57 (12.95)	117.30 (11.12)	120.62 (13.05)	119.76 (15.36)
Mean change (SD)	-3.24 (12.50)	0.13 (11.85)	-0.18 (12.51)	0.42 (12.53)
p-value (active vs placebo)		.176	.098	.052
Diastolic blood pressure (mmHg)	n=86	n=84	n=87	n=85
Mean baseline (SD)	75.60 (9.57)	75.49 (8.87)	77.94 (9.43)	77.18 (10.17)
Mean change (SD)	-0.47 (8.61)	2.11 (9.04)	0.20 (7.33)	0.34 (9.97)
p-value (active vs placebo)		.045	.563	.527
Weight (kg)	n=87	n=84	n=86	n=85
Mean baseline (SD)	80.61 (18.87)	82.08 (20.31)	83.16 (20.95)	89.77 (79.45)
Mean change (SD)	0.47 (1.95)	-0.02 (2.08)	-0.60 (2.20)	-0.41 (2.63)
p-value (active vs placebo)		.149	.002	.010

Abbreviations: Dulox 20 BID = duloxetine 20 mg twice daily; Dulox 40 BID = duloxetine 40 mg twice daily; n = number of patients; Parox 20 QD = paroxetine 20 mg once daily; SD = standard deviation.

Table HMATb.8. Treatment-Emergent Abnormal Electrocardiograms
All Randomized Patients
Acute Therapy Phase

Therapy	N	Abnormal ECG n(%)	Fisher's Exact Pairwise p-Values vs. 1)	vs. 2)	vs. 3)
1)PLACEBO	56	10(18%)			
2)DLX20BID	48	11(23%)	.626		
3)DLX40BID	52	10(19%)	1.00	.807	
4)PRX20QD	48	10(21%)	.804	1.00	1.00

Fisher's Exact p-value overall = 0.9436
Program: RMP.F1JSHMAT.SASPGM.STUDYB(FQECGB1B) QCA70
Data: RMP.SAS.F1JM.MCHMATSW.STUDYB

Table HMATb.9. Summary of Arizona Sexual Experiences Scale
Change from Baseline to Endpoint
All Randomized Patients
Acute Therapy Phase

	Treatment Group			
Variable	Placebo	Dulox 20	Dulox 40	Paroxetine
ASEX Total Score	n=49	n=50	n=45	n=48
Mean baseline (SD)	16.20 (5.06)	15.90 (4.10)	16.36 (3.90)	15.96 (4.74)
Mean change (SD)	0.02 (3.94)	0.50 (3.88)	0.62 (4.80)	0.56 (5.13)
LS Means p-value (active vs placebo)		0.496	0.553	.728
ASEX sum of items 1 and 2	n=85	n=80	n=83	n=72
Mean baseline (SD)	7.53 (2.78)	7.55 (2.45)	7.58 (2.02)	7.60 (2.58)
Mean change (SD)	0.13 (2.06)	-0.24 (2.19)	0.02 (2.07)	-0.10 (2.29)
LS means p-value (active vs placebo)		.277	.850	.667

Abbreviations: ASEX = Arizona Sexual Experiences Scale; Dulox 20 BID = duloxetine 20 mg twice daily; Dulox 40 BID = duloxetine 40 mg twice daily; n = number of patients; Parox 20 QD = paroxetine 20 mg once daily; SD = standard deviation.