COVID-19 is an emerging, rapidly evolving situation.
Get the latest public health information from CDC: https://www.coronavirus.gov.
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Trial record **1 of 1** for: F1J-US-HMFR

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Duloxetine for Multiple Sclerosis Pain

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT00755807

Recruitment Status : Completed
First Posted : September 19, 2008
Results First Posted : December 9, 2011
Last Update Posted : December 9, 2011

Sponsor:
Eli Lilly and Company

Information provided by (Responsible Party):
Eli Lilly and Company

Study Details | Tabular View | Study Results | Disclaimer

How to Read a Study Record

Study Type	Interventional
Study Design	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition	Multiple Sclerosis
Interventions	Drug: Duloxetine Hydrochloride (HCl) Drug: Placebo
Enrollment	239

Participant Flow

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Recruitment Details	
Pre-assignment Details	

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period. If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).	Participants received placebo po, QD for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Period Title: **Acute Phase**		
Started	118	121
Completed	100	109

Not Completed	18	12
Reason Not Completed		
Adverse Event	16	5
Protocol Violation	1	3
Withdrawal by Subject	1	2
Lack of Efficacy	0	1
Physician Decision	0	1
Period Title: **Open-label Extension Phase**		
Started	100	109
Completed	82	93
Not Completed	18	16
Reason Not Completed		
Adverse Event	7	7
Protocol Violation	5	2
Lack of Efficacy	3	3
Withdrawal by Subject	1	3
Lost to Follow-up	2	0
Sponsor Decision	0	1

Baseline Characteristics

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Arm/Group Title	Duloxetine	Placebo	Total
Arm/Group Description	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period. If the participant completes the	Participants received placebo po, QD for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the	Total of all reporting groups

		6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).	open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).	
Overall Number of Baseline Participants		118	121	239
▼ Baseline Analysis Population Description		[Not Specified]		
Age Continuous Mean (Standard Deviation) Unit of measure: Years				
	Number Analyzed	118 participants	121 participants	239 participants
		50.77 (9.67)	52.67 (9.07)	51.73 (9.40)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: Participants				
	Number Analyzed	118 participants	121 participants	239 participants
	Female	86 72.9%	93 76.9%	179 74.9%
	Male	32 27.1%	28 23.1%	60 25.1%

Race/Ethnicity, Customized Measure Type: Number Unit of measure: Participants	Number Analyzed	118 participants	121 participants	239 participants
African		9	6	15
Caucasian		109	112	221
Hispanic		0	2	2
Native American		0	1	1
Region of Enrollment Measure Type: Number Unit of measure: Participants	Number Analyzed	118 participants	121 participants	239 participants
Belgium		7	7	14
Canada		4	7	11
Poland		20	20	40
United States		87	87	174
Multiple Sclerosis (MS) Diagnosis Subtype [1] Measure Type: Number Unit of measure: Participants	Number Analyzed	118 participants	121 participants	239 participants
Primary-Progressive		10	16	26
Progressive-Relapsing		4	6	10
Relapsing-Remitting		81	72	153
		23	27	50

Secondary-Progressive				

[1] Measure Description:
National MS Society diagnosis subtypes:

Primary progressive: initially progressive disease with no plateaus or remissions; or occasional plateau and acute, minor improvements.

Progressive-relapsing: initial disease progression, but with clear, acute relapses, with or without full recovery from such relapses over time.

Relapsing-remitting: clearly defined acute attacks with full or partial recovery; no disease progression between attacks.

Secondary-progressive: initially relapsing-remitting, then progressive at a variable rate, with possible occasional relapse and minor remission.

Duration of MS [1]
Mean (Standard Deviation)
Unit of measure: Years

Number Analyzed	118 participants	121 participants	239 participants
	11.05 (7.48)	11.40 (8.49)	11.23 (7.99)

[1] Measure Description: How long the participants have had MS.

Duration of central neuropathic pain (CNP) due to MS (n=118, 120) Mean (Standard Deviation)				

Unit of measure: Years				
	Number Analyzed	118 participants	121 participants	239 participants
		6.18 (5.88)	7.56 (6.69)	6.88 (6.33)
Weekly 24-Hour Average Pain [1] Mean (Standard Deviation) Unit of measure: Units on a scale				
	Number Analyzed	118 participants	121 participants	239 participants
		6.49 (1.41)	6.31 (1.33)	6.40 (1.37)
Brief Pain Inventory (BPI) Average Interference (Duloxetine n=116, Placebo n=119) [1] Mean (Standard Deviation) Unit of measure: Units on a scale				
	Number Analyzed	118 participants	121 participants	239 participants
		5.50 (1.98)	5.24 (2.01)	5.37 (2.00)

[1] Measure Description: This is an ordinal scale with scores from 0 (no pain) to 10 (worst possible pain). Data presented represent the weekly mean of the scores of the average pain severity over the last 24 hours. Scores are based on daily assessments recorded by participants in their diaries.

		[1] Measure Description: A self-reported scale that measures interference of pain on average of the 7 questions assessing the interference of pain for general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life. The average Interference scores range from 0 (does not interfere) to 10 (completely interferes).		
BPI Average Pain (Duloxetine n=116, Placebo n=119) [1] Mean (Standard Deviation) Unit of measure: Units on a scale				
	Number Analyzed	118 participants	121 participants	239 participants
		6.09 (1.50)	5.91 (1.33)	6.00 (1.42)
		[1] Measure Description: A self-reported scale that measures the severity of pain based on the average pain over the past 24-hours. The severity scores range from 0 (no pain) to 10 (pain as severe as you can imagine).		
Multiple Sclerosis Quality of Life (MS-QOL-54) Overall Quality of Life Subsection [1] Mean (Standard Deviation) Unit of measure: Units on a scale				
		118 participants	121 participants	239 participants

	Number Analyzed			
		58.06 (18.61)	61.78 (18.80)	59.94 (18.76)

[1] Measure Description: The MS-QOL-54 is self-reported and consists of 54 questions covering 12 domains: physical function, role limitations due to physical problems, role limitations due to emotional problems, emotional wellbeing, energy, health perceptions, social function, cognitive function, health distress, satisfaction with sexual function, change in health, and overall quality of life. Each domain score is converted into a 0-100 score based on the individual item responses, with higher scores indicating better health status or functioning. Number of participants (n) for duloxetine=116; placebo=119.

Expanded Disability Status Scale ([EDSS], n=118, 120) [1]
Median (Standard Deviation)
Unit of measure: Units on a scale

Number Analyzed	118 participants	121 participants	239 participants
	4.00 (2.01)	4.00 (1.78)	4.00 (1.89)

	[1] Measure Description: The EDSS is a method of quantifying disability in multiple sclerosis. The EDSS quantifies disability in 8 Functional Systems (pyramidal, cerebellar, brain stem, sensory, bowel and bladder, visual, cerebral, and other) and allows neurologists to assign a functional system score in each. An EDSS of 0.0 is a normal neurological examination. The scores increase in increments of 0.5 starting with 1.0 (no disability, minimal signs in 1 functional system) to 10.0 (death due to MS).

Outcome Measures

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1. Primary Outcome

Title	Change From Baseline in the Weekly 24-Hour Average Pain Scores at Week 6 (Acute Phase)
Description	24-hour average pain severity scores recorded daily on an 11-point Likert scale, evaluated as a weekly mean, with scores ranging from 0 (no pain) to 10 (worst possible pain). Participants should complete electronic diary each day upon awakening. The 11-point Likert scale was used for assessment of 24-hour average pain and evaluated as weekly means. Scores range from 0 (no pain) to 10 (worst possible pain). The Least Squares Mean (LS Mean) Value was adjusted for investigative site and baseline severity.
Time Frame	Baseline, 6 weeks

Outcome Measure Data

Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine	

	(oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
Overall Number of Participants Analyzed	103	115
Least Squares Mean (Standard Error) Unit of Measure: units on a scale		
	-1.83 (0.17)	-1.07 (0.16)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	Null hypothesis: no difference measured by weekly mean of t 6 weeks. Sample size is deterr of randomized participants with 119 participants per arm, study on treatment group difference.
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.001
	Comments	The a priori threshold for statis
	Method	Mixed Models Analysis
	Comments	Mixed model repeated measur Baseline=Baseline+Treatment random effect.

2. Secondary Outcome

Title	Change From Baseline in the Weekly 24-Hour Average Pain Scores up to Week 6 (Acute Phase)

▼ Description	This is a nominal outcome reflecting whether or not a clinically-important efficacy outcome (≥30% or ≥50% pain reduction from baseline) was achieved at endpoint. It is based on a comparison between baseline and endpoint scores on an ordinal scale with scores from 0 (no pain) to 10 (worst possible pain). Used were the weekly mean of the scores of the average pain severity over the last 24 hours. The weekly averages were based on daily assessments recorded by participants in their diaries.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value. Last-observation-carried-forward (LOCF) imputation was implemented for participants with early discontinuation. Baseline-observation-carried-forward (BOCF) imputation was implemented for participants with early discontinuation.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
Overall Number of Participants Analyzed	115	119
Measure Type: Number Unit of Measure: participants		
≥30% Reduction (LOCF)	47	32
≥50% Reduction (LOCF)	26	19

≥30% Reduction (BOCF)	44	29
≥50% Reduction (BOCF)	24	16

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.027
	Comments	P-value is for the 30% Reduction (LOCF). P-values were not adjusted for multiple comparisons; a priori threshold for statistical significance was 0.05.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.246
	Comments	P-value is for 50% Reduction (LOCF). P-values were not adjusted for multiple comparisons; a priori threshold for statistical significance was 0.05.

	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.024
	Comments	P-value is for the 30% Reduction (BOCF). P-values were not adjusted for multiple comparisons; a priori threshold for statistical significance was 0.05.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.165
	Comments	P-value is for 50% Reduction (BOCF). P-values were not adjusted for multiple comparisons; a priori threshold for statistical significance was 0.05.
	Method	Fisher Exact
	Comments	[Not Specified]

3. Secondary Outcome

Title	Patient Global Impressions of Improvement Scale (PGI-I) at 6 Weeks
▼ Description	A scale that measures the participant's perception of improvement at the time of assessment compared with the start of treatment. The score ranges from 1 (very much better) to 7 (very much worse). The Least Squares (LS) Mean Value was adjusted for investigative site and baseline severity.
Time Frame	6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with at least 1 post-baseline value. Last-observation-carried-forward (LOCF) imputation was implemented.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
Overall Number of Participants Analyzed	106	116
Least Squares Mean (Standard Error) Unit of Measure: units on a scale		
	3.27 (0.11)	3.48 (0.10)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo

	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.121
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANOVA
	Comments	Analysis of Variance (ANOVA) Model: PGI improvement at Endpoint = Treatment + Investigator.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.21
	Confidence Interval	(2-Sided) 95% -0.06 to 0.49
	Estimation Comments	The mean difference is for placebo - duloxetine.

4. Secondary Outcome

Title	Change From Baseline in the Brief Pain Inventory Severity and Interference Scores (BPI-S/BPI-I) at Week 6 (Acute Phase)
▼ Description	Measures pain severity and interference on function. Severity scores: 0 (no pain) to 10 (severe pain) on each question assessing worst, least, and average pain in past 24 hours, and pain right now. Interference scores: 0 (does not interfere) to 10 (completely interferes) on each question assessing pain interference in past 24 hours, such as general activity, mood, normal work, relations with other people, and sleep. Average interference=average of non-missing scores of individual interference items. Least Squares (LS) Mean Value was adjusted for investigative site and baseline severity.

Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	106	116
Least Squares Mean (Standard Error) Unit of Measure: units on a scale		
BPI Severity for Worst Pain	-1.95 (0.21)	-1.29 (0.20)
BPI Severity for Least Pain	-1.20 (0.18)	-0.72 (0.17)
BPI Severity for Average Pain	-1.36 (0.19)	-0.84 (0.17)
BPI Severity for Pain Right Now	-1.91 (0.21)	-1.02 (0.20)
BPI Interference for General Activity	-1.81 (0.23)	-1.29 (0.22)

BPI Interference for Mood	-1.91 (0.24)	-1.25 (0.22)
BPI Interference for Walking Ability	-1.47 (0.25)	-0.91 (0.24)
BPI Interference for Normal Work	-1.51 (0.24)	-1.18 (0.22)
BPI Interference for Relations With Others	-1.72 (0.22)	-1.22 (0.20)
BPI Interference for Sleep	-2.01 (0.22)	-1.59 (0.21)
BPI Interference for Enjoyment Of Life	-1.82 (0.24)	-1.65 (0.23)
BPI Mean Interference Score	-1.77 (0.19)	-1.32 (0.18)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.016
	Comments	P-value is for BPI Severity for Worst Pain score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
	Estimation Parameter	

Method of Estimation		Mean Difference (Final Values)
	Estimated Value	0.66
	Confidence Interval	(2-Sided) 95% 0.12 to 1.20
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.043
	Comments	P-value is for BPI Severity for Least Pain score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.48
	Confidence Interval	(2-Sided) 95% 0.02 to 0.95
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.030
	Comments	P-value is for BPI Severity for Average Pain score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.52
	Confidence Interval	(2-Sided) 95% 0.05 to 0.99
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.001
	Comments	P-value is for BPI Severity for Pain Right Now score.

		P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.89
	Confidence Interval	(2-Sided) 95% 0.36 to 1.43
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.083
	Comments	P-value is for BPI Interference for General Activity score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment +

		Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.52
	Confidence Interval	(2-Sided) 95% -0.07 to 1.11
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.034
	Comments	P-value is for BPI Interference for Mood score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.66
	Confidence Interval	(2-Sided) 95% 0.05 to 1.27
	Estimation Comments	

		The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.089
	Comments	P-value is for BPI Interference for Walking Ability score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.55
	Confidence Interval	(2-Sided) 95% -0.08 to 1.19
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	0.291
	Comments	P-value is for BPI Interference for Normal Work score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.33
	Confidence Interval	(2-Sided) 95% -0.28 to 0.93
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.077
	Comments	P-value is for BPI Interference for Relations With Others score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.

	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.50
	Confidence Interval	(2-Sided) 95% -0.06 to 1.05
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.148
	Comments	P-value is for BPI Interference for Sleep score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.41

	Confidence Interval	(2-Sided) 95% -0.15 to 0.97
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.582
	Comments	P-value is for BPI Interference for Enjoyment Of Life score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.17
	Confidence Interval	(2-Sided) 95% -0.45 to 0.79
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]

	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.067
	Comments	P-value is for BPI Mean Interference score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.45
	Confidence Interval	(2-Sided) 95% -0.03 to 0.94
	Estimation Comments	The mean difference is for placebo - duloxetine.

5. Secondary Outcome

Title	Change From Baseline in the Clinical Global Impression of Severity Scale (CGI-S) at 6 Weeks (Acute Phase)
▼ Description	Measures severity of illness at the time of assessment compared with start of treatment. Scores range from 1 (normal, not at all ill) to 7 (among the most extremely ill participants). The Least Squares (LS) Mean Value was adjusted for investigative site and baseline severity.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
Overall Number of Participants Analyzed	111	114
Least Squares Mean (Standard Error) Unit of Measure: units on a scale		
	-0.67 (0.09)	-0.44 (0.08)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.041
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.23
	Confidence Interval	(2-Sided) 95% 0.01 to 0.45
	Estimation Comments	The mean difference is for placebo - duloxetine.

6. Secondary Outcome

Title	Change From Baseline in the Multiple Sclerosis Quality of Life-54 Instrument (MS-QOL-54) at 6 Weeks (Acute Phase)
▼ Description	A 54 question measure covers 12 domains; assesses mental and physical health. Each domain score is converted into a 0-100 score based on individual item responses; higher scores=better health status. The physical health composite score is a weighted average of the physical health scales, such as physical function, health perceptions, and energy. The mental health composite score is a weighted average of the mental health scales, such as overall quality of life, cognitive function, and health distress. The Least Squares (LS) Mean Value was adjusted for investigative site and baseline severity.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
	106	116

Overall Number of Participants Analyzed		
Least Squares Mean (Standard Error) Unit of Measure: units on a scale		
Physical Health Composite (N=106, 116)	6.11 (1.15)	5.12 (1.08)
Mental Health Composite (N=106, 116)	5.81 (1.44)	4.59 (1.35)
Physical Health (N=106, 116)	3.35 (1.51)	2.65 (1.42)
Health Perceptions (N=106, 116)	1.41 (1.39)	1.35 (1.31)
Energy Subsection Score (N=106, 116)	6.54 (1.60)	6.51 (1.50)
Role Limitation Due to Physical (N=106, 116)	11.73 (3.17)	8.60 (2.97)
Pain (N=106, 116)	12.42 (1.72)	8.84 (1.62)
Sexual Function (N=106, 116)	1.30 (2.21)	1.12 (2.09)
Social Function (N=106, 116)	5.02 (1.71)	6.97 (1.61)
Health Distress (N=106, 116)	8.96 (1.76)	9.34 (1.66)
Overall Quality Of Life (N=106, 116)	3.66 (1.34)	5.43 (1.26)
Emotional Well-being Subsection Score (N=106, 116)	4.59 (1.37)	3.99 (1.29)
	6.48 (3.55)	1.58 (3.33)

Role Limitation Due to Emotional (N=106, 116)		
Cognitive Function (N=106, 116)	6.38 (1.45)	5.57 (1.36)
Change in Health (N=106, 116)	8.23 (2.30)	6.25 (2.16)
Satisfaction with Sexual Function (N=102, 112)	2.66 (2.82)	-1.35 (2.68)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.500
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Physical Health Composite Section score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.00

	Confidence Interval	(2-Sided) 95% -3.90 to 1.91
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.512
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Mental Health Composite Section score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.22
	Confidence Interval	(2-Sided) 95% -4.87 to 2.44
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.720
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Physical Health Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.69
	Confidence Interval	(2-Sided) 95% -4.51 to 3.12
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	0.973
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Health Perceptions Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.06
	Confidence Interval	(2-Sided) 95% -3.58 to 3.46
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.991
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Energy Subsection score. P-values are not adjusted

		for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.02
	Confidence Interval	(2-Sided) 95% -4.07 to 4.02
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.441
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Role Limitation Due to Physical Problems Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA

	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3.14
	Confidence Interval	(2-Sided) 95% -11.14 to 4.87
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.108
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Pain Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3.58

	Confidence Interval	(2-Sided) 95% -7.94 to 0.79
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.948
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Sexual Function Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.19
	Confidence Interval	(2-Sided) 95% -5.77 to 5.39
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.374
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Social Function Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	1.96
	Confidence Interval	(2-Sided) 95% -2.37 to 6.28
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	0.867
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Health Distress Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.38
	Confidence Interval	(2-Sided) 95% -4.10 to 4.87
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.306
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Overall Quality Of Life Subsection score. P-values are not adjusted

		for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	1.77
	Confidence Interval	(2-Sided) 95% -1.63 to 5.17
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.733
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Emotional Well-being Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	

		Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.60
	Confidence Interval	(2-Sided) 95% -4.08 to 2.88
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.283
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Role Limitation Due to Emotional Problems score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)

	Estimated Value	-4.90
	Confidence Interval	(2-Sided) 95% -13.88 to 4.08
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.664
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Cognitive Function Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.81
	Confidence Interval	(2-Sided) 95% -4.49 to 2.86
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.504
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Change in Health Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.98
	Confidence Interval	(2-Sided) 95% -7.81 to 3.85
	Estimation Comments	The mean difference is for placebo - duloxetine

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	0.270
	Comments	P-value is for treatment comparison of change from baseline on MSQOL Satisfaction with Sexual Function Subsection score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-4.02
	Confidence Interval	(2-Sided) 95% -11.18 to 3.14
	Estimation Comments	The mean difference is for placebo - duloxetine

7. Secondary Outcome

Title	Number of Participants With Suicidal Behaviors, Ideations, and Acts Based on The Columbia Suicide Severity Rating Scale (C-SSRS) at Week 6
▼ Description	C-SSRS scale captures occurrence, severity, and frequency of suicide-related thoughts and behaviors. Number of participants with suicidal behaviors, ideations, and acts are provided. Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide. Suicidal ideation: a "yes" answer to any one of 5 suicidal ideation questions, which includes wish to be dead, and 4

	different categories of active suicidal ideation. Suicidal act: a "yes" answer to actual attempt or completed suicide.
Time Frame	6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
Overall Number of Participants Analyzed	118	121
Measure Type: Number Unit of Measure: participants		
Suicidal Ideation	3	0
Suicidal Behavior	1	0
Suicidal Acts	1	0

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.119
	Comments	P-value is for treatment comparison in number of

		participants with CSSR-S Suicidal Ideation during first 6 weeks of acute treatment. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.494
	Comments	P-value is for treatment comparison in number of participants with CSSR-S Suicidal Behavior during first 6 weeks of acute treatment. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other

	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.494
	Comments	P-value is for treatment comparison in number of participants with CSSR-S Suicidal Acts during first 6 weeks of acute treatment. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Fisher Exact
	Comments	[Not Specified]

8. Secondary Outcome

Title	Change From Baseline in the Weekly Mean of Night Pain Scores at Week 6 (Acute Phase)
▼ Description	Weekly mean of the night pain severity scores recorded daily on an 11-point Likert scale, an ordinal scale ranging from 0 (no pain) to 10 (worst possible pain). Participants should complete the electronic diary each day upon awakening. The Least Squares (LS) Mean Value was adjusted for investigative site and baseline severity.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at	Participants received placebo (po, QD) for 6 weeks (acute phase).

	60 mg in the acute placebo-controlled period.	
Overall Number of Participants Analyzed	115	119
Least Squares Mean (Standard Error) Unit of Measure: units on a scale		
	-1.25 (0.12)	-0.74 (0.12)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.002
	Comments	P-values are not adjusted for n statistical significance was 0.0
	Method	Mixed Models Analysis
	Comments	Mixed model repeated measur Baseline=Baseline+Treatment participant=random effect.

9. Secondary Outcome

Title	Change From Baseline in the Beck Depression Inventory II (BDI-II) Question #9 at Week 6 (Acute Phase)
▼ Description	The BDI-II is completed by the participant to rate the severity of depressive symptoms and any improvement during the course of the trial. The total score ranges from 0 to 63 with higher the score indicating more severe depressive symptoms. Question #9 is suicidal thoughts and wishes with a score ranging from 0 to 3.

Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
Overall Number of Participants Analyzed	105	115
Mean (Standard Deviation) Unit of Measure: units on a scale		
	-0.04 (0.39)	-0.03 (0.21)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.662
	Comments	P-value is for treatment comparison of change from baseline on BDI-II Question #9 score. P-values are not adjusted for multiple comparisons.

		The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.01
	Confidence Interval	(2-Sided) 95% -0.06 to 0.04
	Estimation Comments	The mean difference is for placebo - duloxetine.

10. Secondary Outcome

Title	Number of Participants Who Discontinued During the Acute Phase (by Week 6)
▼ Description	[Not Specified]
Time Frame	Baseline through 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase).
	118	121

Overall Number of Participants Analyzed		
Measure Type: Number Unit of Measure: participants		
Discontinued Due to Any Reason	18	12
Adverse Event (AE)	16	5
Protocol Violation	1	3
Subject Decision	1	2
Lack of Efficacy	0	1
Physician Decision	0	1

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.244
	Comments	This is the P-value for Discontinuation Due to Any Reason.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
	P-Value	0.012

Statistical Test of Hypothesis	Comments	This is the P-value for Adverse Event (AE).
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.622
	Comments	This is the P-value for Protocol Violation.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	1.00
	Comments	This is the P-value for Subject Decision.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	This is the P-value for Lack of Efficacy.
	Method	Fisher Exact
	Comments	[Not Specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	1.00
	Comments	This is the P-value for Physician Decision.
	Method	Fisher Exact
	Comments	[Not Specified]

11. Secondary Outcome

Title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) During the Acute Phase
▼ Description	Summary tables of serious adverse events (SAEs) and all other non-serious adverse events are located in the Reported Adverse Event Module.
Time Frame	Baseline through 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant

	1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	118	121
Measure Type: Number Unit of Measure: participants		
Adverse Events (AEs) - Any Event	70	59
Serious Adverse Events (SAEs) - Any Event	4	0

12. Secondary Outcome

Title	Number of Participants With Adverse Events (AEs) Resulting in Discontinuation From Baseline During the Acute Phase
▼ Description	[Not Specified]
Time Frame	Baseline through 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-

	60 mg in the acute placebo-controlled period.	blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	118	121
Measure Type: Number Unit of Measure: participants		
Any Adverse Event (AE)	16	5
Dizziness	3	1
Somnolence	2	0
Abdominal discomfort	1	0
Asthenia	1	0
Back pain	1	0
Balance disorder	0	1
Fear	1	0
Feeling jittery	1	0
Headache	0	1
Hypotension	0	1
Libido decreased	1	0
Mood altered	0	1
Nausea	1	0
Pain in extremity	1	0
Rash maculo-papular	1	0
Suicide attempt	1	0
Throat irritation	1	0

13. Secondary Outcome

Title	Change From Baseline in Blood Pressure at Week 6 (Acute Phase)
▼ Description	[Not Specified]
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	112	119
Least Squares Mean (Standard Error) Unit of Measure: mm Hg		
Diastolic Blood Pressure	1.34 (0.66)	0.48 (0.63)
Systolic Blood Pressure	0.34 (1.14)	-0.06 (1.09)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.322
	Comments	P-value is for treatment comparison of change from baseline on diastolic blood pressure. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.86
	Confidence Interval	(2-Sided) 95% -2.55 to 0.84
	Estimation Comments	The mean difference is for placebo - duloxetine.

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
	P-Value	0.787

	Statistical Test of Hypothesis	Comments	P-value is for treatment comparison of change from baseline on systolic blood pressure. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
		Method	ANCOVA
		Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
	Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
		Estimated Value	-0.40
		Confidence Interval	(2-Sided) 95% -3.32 to 2.52
		Estimation Comments	The mean difference is for placebo - duloxetine.

14. Secondary Outcome

Title	Change From Baseline in Pulse Rate at Week 6 (Acute Phase)
▼ Description	[Not Specified]
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant

	1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	112	118
Least Squares Mean (Standard Error) Unit of Measure: beats per minute (bpm)		
	1.76 (0.84)	0.22 (0.81)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.160
	Comments	P-value is for treatment comparison of change from baseline on pulse rate. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment +

		Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.55
	Confidence Interval	(2-Sided) 95% -3.70 to 0.61
	Estimation Comments	The mean difference is for placebo - duloxetine.

15. Secondary Outcome

Title	Change From Baseline in Weight at Week 6 (Acute Phase)
▼ Description	[Not Specified]
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	99	115

Least Squares Mean (Standard Error) Unit of Measure: kilograms (kg)		
	-0.69 (0.20)	0.08 (0.18)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.003
	Comments	P-value is for treatment comparison of change from baseline on weight. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANCOVA
	Comments	Model: Change from Baseline = Treatment + Investigator + Baseline Value.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.77
	Confidence Interval	(2-Sided) 95% 0.27 to 1.26
	Estimation Comments	The mean difference is for placebo - duloxetine.

16. Secondary Outcome

Title	Patient Global Impressions of Improvement Scale (PGI-I) Score at 18 Weeks
▼ Description	A scale that measures the participant's perception of improvement at the time of assessment compared with the start of treatment. The scores range from 1 (very much better) to 7 (very much worse).
Time Frame	18 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	204
Mean (Standard Deviation) Unit of Measure: units on a scale	
	2.67 (1.25)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	

			P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
		Method	t-test, 2 sided
		Comments	One-sample t-test of mean PGI-I score at 18 weeks for all participants who entered extension phase.

17. Secondary Outcome

Title	Change From Baseline in Brief Pain Inventory Severity and Interference Scores (BPI-S/BPI-I) at Week 18
▼ Description	BPI-S and BPI-I are self-reported scales measuring severity of pain and interference on function. Severity scores: 0 (no pain) to 10 (severe pain) on each question assessing worst pain, least pain, and average pain in past 24 hours, and pain right now. Interference scores: 0 (does not interfere) to 10 (completely interferes) on each question assessing interference of pain in past 24 hours for general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life. Average interference = average of non-missing scores of individual interference items.
Time Frame	Baseline (end of acute phase/Week 6), Endpoint (Week 18)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).

Overall Number of Participants Analyzed	201
Mean (Standard Deviation) Unit of Measure: units on a scale	
BPI-S for Worst Pain	-1.27 (2.07)
BPI-S for Least Pain	-0.96 (1.84)
BPI-S for Average Pain	-1.26 (1.76)
BPI-S for Pain Right Now	-1.03 (2.20)
BPI-I for General Activity	-1.01 (2.50)
BPI-I for Mood	-1.08 (2.56)
BPI-I for Walking Ability	-0.84 (2.62)
BPI-I for Normal Work	-1.00 (2.60)
BPI-I for Relations With Others	-0.65 (2.59)
BPI-I for Sleep	-0.70 (2.37)
BPI-I for Enjoyment Of Life	-1.03 (2.47)
BPI for Mean Interference Score	-0.89 (2.06)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for BPI-S for Worst Pain. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-S for Worst Pain.

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for BPI-S for Least Pain. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-S for Least Pain score.

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for BPI-S for Average Pain. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-S for Average Pain score.

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint

		on BPI-S for Pain Right Now score.

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for BPI-I for General Activity. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-I for General Activity score.

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for the BPI-I for Mood. P-values are not adjusted for multiple comparisons. The a priori

		threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-I for Mood score.

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for the BPI-I for Walking Ability. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-I for Walking Ability score.

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
	P-Value	<0.001

Statistical Test of Hypothesis	Comments	The P-value is for the BPI-I for Normal Work. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-I for Normal Work score.

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for the BPI-I for Relations With Others. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from baseline to endpoint on BPI-I for Relations With Others score.

▼ Statistical Analysis 10

		Duloxetine

Statistical Analysis Overview	Comparison Group Selection	
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for the BPI-I for Sleep. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI-I for Sleep score.

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for the BPI-I for Enjoyment of Life. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint

		on BPI-I for Enjoyment Of Life score.

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	The P-value is for the BPI for Mean Interference Score. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on BPI for Mean Interference score.

18. Secondary Outcome

Title	Change From Baseline in the Clinical Global Impression of Severity Scale (CGI-S) Score at Week 18 (Open-label Extension Phase)
▼ Description	Measures severity of illness at the time of assessment compared with start of treatment. Scores range from 1 (normal, not at all ill) to 7 (among the most extremely ill participants).
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	206
Mean (Standard Deviation) Unit of Measure: units on a scale	
	-0.59 (1.02)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on CGI-S score for all participants who entered extension phase.

19. Secondary Outcome

Title	Change From Baseline in Multiple Sclerosis Quality of Life-54 Instrument (MS-QOL-54) at Week 18 (Open-label Extension Phase)
▼ Description	A 54 question measure covers 12 domains; assesses mental and physical health. Each domain score is converted into a 0-100 score based on individual item responses; higher scores=better health status. The physical health composite score is a weighted average of the physical health scales, such as physical function, health perceptions, and energy. The mental health composite score is a weighted average of the mental health scales, such as overall quality of life, cognitive function, and health distress.
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	201
Mean (Standard Deviation) Unit of Measure: units on a scale	
Physical Health Composite Section Score (N=198)	2.70 (12.32)
	1.97 (14.45)

Mental Health Composite Section Score (N=201)	
Physical Health Subsection Score (N=201)	3.16 (14.29)
Health Perceptions Subsection Score (N=201)	2.24 (14.04)
Energy Subsection Score (N=201)	2.93 (15.42)
Role Limitation Due to Physical Problems (N=201)	0.50 (39.29)
Pain Subsection Score (N=201)	7.45 (17.57)
Sexual Function Subsection Score (N=198)	0.79 (23.38)
Social Function Subsection Score (N=201)	2.53 (18.30)
Health Distress Subsection Score (N=201)	1.44 (18.51)
Overall Quality Of Life Subsection Score (N=201)	1.47 (11.04)
Emotional Well-being Subsection Score (N=201)	2.63 (13.61)
Role Limitation Due to Emotional Problems (N=201)	3.15 (38.96)
	-0.07 (14.64)

Cognitive Function Subsection Score (N=201)	
Change in Health Subsection Score (N=201)	4.35 (25.30)
Satisfaction with Sexual Function Subsect (N=195)	1.92 (30.56)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.002
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Physical Health Composite Section score.

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	0.054
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Mental Health Composite Section score.

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.002
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Physical Health Subsection score.

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]

	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.025
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Health Perceptions Subsection score.

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.008
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Energy Subsection score.

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.858
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Role Limitation Due to Physical Problems Subsection score.

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint

		on MSQOL Pain Subsection score.

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.637
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Sexual Function Subsection score.

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.051
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided

	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Social Function Subsection score.

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.270
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Health Distress Subsection score.

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.061
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for

		statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Overall Quality Of Life Subsection score.

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.007
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Emotional Well-being Subsection score.

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
	P-Value	0.253

Statistical Test of Hypothesis	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Role Limitation Due to Emotional Problems score.

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.942
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Cognitive Function Subsection score.

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Group Selection	Duloxetine

	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.016
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Change in Health Subsection score.

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.381
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on MSQOL Satisfaction with Sexual Function Subsection score.

20. Secondary Outcome

Title	Number of Participants With Suicidal Behaviors, Ideations, and Acts Based on The Columbia Suicide Severity Rating Scale (C-SSRS) at Week 18
▼ Description	C-SSRS scale captures occurrence, severity, and frequency of suicide-related thoughts and behaviors. Number of participants with suicidal behaviors, ideations, and acts are provided. Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide. Suicidal ideation: a "yes" answer to any one of 5 suicidal ideation questions, which includes wish to be dead, and 4 different categories of active suicidal ideation. Suicidal act: a "yes" answer to actual attempt or completed suicide.
Time Frame	18 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants who entered the extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	209
Measure Type: Number Unit of Measure: participants	
Suicidal Ideation	1
Suicidal Behavior	0
Suicidal Acts	0

21. Secondary Outcome

Title	Change in the Weekly Mean of the Night Pain Scores From Week 6 Through Week 18 (Open-label Extension Phase)
▼ Description	Weekly mean of the night pain severity scores recorded daily on an 11-point Likert scale, an ordinal scale ranging from 0 (no pain) to 10 (worst possible pain). Participants should complete the electronic diary each day upon awakening. Each weekly mean change represents change relative to week 6, the baseline of the extension phase.
Time Frame	Baseline (6 weeks) through Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	206
Least Squares Mean (Standard Error) Unit of Measure: units on a scale	
Week 7 (n=185)	-0.05 (0.07)
Week 8 (n=205)	-0.31 (0.07)
Week 9 (n=184)	-0.54 (0.08)
Week 10 (n=197)	-0.62 (0.08)
Week 11 (n=166)	-0.75 (0.08)
Week 12 (n=192)	-0.89 (0.09)
Week 13 (n=166)	-1.05 (0.09)
Week 14 (n=177)	-0.98 (0.10)

Week 15 (n=158)	-0.99 (0.11)
Week 16 (n=176)	-1.04 (0.11)
Week 17 (n=156)	-1.11 (0.11)
Week 18 (n=175)	-1.04 (0.11)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.524
	Comments	P-value is for test of mean c phase baseline to endpoint (adjusted for multiple compar threshold for statistical signi
	Method	Mixed Models Analysis
	Comments	Mixed model repeated meas Change from Baseline=Baseline+Investig participant was treated as ra

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 8). P-values are not adjusted for multiple comparisons. The a priori

		threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 9). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Group Selection	Duloxetine

	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 10). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 11). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	

		MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 12). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 13). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 14). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week +

		Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 15). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension

		phase baseline to endpoint (Week 16). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 17). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	P-value is for test of mean change from extension phase baseline to endpoint (Week 18). P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Mixed Models Analysis
	Comments	MMRM Model: Change from Baseline = Baseline + Investigator + Week + Baseline* Week, where participant was treated as a random effect.

22. Secondary Outcome

Title	Change From Baseline in Beck Depression Inventory II (BDI-II), Question #9 at Week 18 (Open-label Extension Phase)
▼ Description	The BDI-II is completed by the participant to rate the severity of depressive symptoms and any improvement during the course of the trial. The total score ranges from 0 to 63 with higher the score indicating more severe depressive symptoms. Question #9 is suicidal thoughts and wishes with the score ranging from 0 to 3.
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	200
Mean (Standard Deviation) Unit of Measure: units on a scale	
	-0.01 (0.19)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.706
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	1-sample t-test of mean change from extension phase baseline to endpoint on BDI-II Question #9 score for all participants

			who entered extension phase.

23. Secondary Outcome

Title	Number of Participants Who Discontinued During the Open-label Extension Phase (by Week 18)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks) through Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
All participants randomized to placebo in acute phase received duloxetine during the extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	209
Measure Type: Number Unit of Measure: participants	
Discontinued Due to Any Reason	34
Adverse Event	14
Protocol Violation	7
Lack of Efficacy	6
Subject Decision	4
Lost to follow up	2
Sponsor Decision	1

24. Secondary Outcome

Title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) During the Open-label Extension Phase
▼ Description	Summary tables of serious adverse events (SAEs) and all other non-serious adverse events are located in the Reported Adverse Event Module.
Time Frame	Baseline (6 weeks) through Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants in the open-label extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	60 mg oral, once daily (QD) for 6-weeks (acute phase) followed by 60, 90, or 120 mg QD for 12-weeks (open label extension phase).
Overall Number of Participants Analyzed	209
Measure Type: Number Unit of Measure: participants	
Adverse Events (AEs) - Any Event	130
Serious Adverse Events (SAEs) - Any Event	7

25. Secondary Outcome

Title	Number of Participants With Adverse Events (AEs) Resulting in Discontinuation During the Open-label Extension Phase
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks) through Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
All randomized participants in the open-label extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	209
Measure Type: Number Unit of Measure: participants	
Due to any AE	14
Fatigue	2
Somnolence	2
Alanine aminotransferase increased	1
Constipation	1
Diverticulitis	1
Dizziness	1
Fall	1
Hypertension	1
Insomnia	1
Multiple sclerosis relapse	1
Nausea	1
Rash pruritic	1

26. Secondary Outcome

Title	

	Change From Baseline in Blood Pressure at Week 18 (Open-label Extension Phase)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	60 mg oral, once daily (QD) for 6-weeks (acute phase) followed by 60, 90, or 120 mg QD for 12-weeks (open label extension phase).
Overall Number of Participants Analyzed	207
Mean (Standard Deviation) Unit of Measure: mm Hg	
Diastolic	-0.58 (8.44)
Systolic	-1.22 (13.07)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.320
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for

		statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on diastolic blood pressure.

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.182
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on systolic blood pressure.

27. Secondary Outcome

Title	Change From Baseline in Pulse Rate at Week 18 (Open-label Extension Phase)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks), endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	60 mg oral, once daily (QD) for 6-weeks (acute phase) followed by 60, 90, or 120 mg QD for 12-weeks (open label extension phase).
Overall Number of Participants Analyzed	207
Mean (Standard Deviation) Unit of Measure: beats per minute (bpm)	
	1.47 (9.81)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.032
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	t-test, 2 sided
	Comments	One-sample t-test of mean change from extension phase baseline to endpoint on pulse rate.

28. Secondary Outcome

Title	Change From Baseline in Weight at Week 18 (Open-label Extension Phase)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	60 mg oral, once daily (QD) for 6-weeks (acute phase) followed by 60, 90, or 120 mg QD for 12-weeks (open label extension phase).
Overall Number of Participants Analyzed	190
Mean (Standard Deviation) Unit of Measure: kilograms (kg)	
	-0.30 (2.84)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.151
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for

	statistical significance was 0.05.
Method	t-test, 2 sided
Comments	One-sample t-test of mean change from extension phase baseline to endpoint on weight.

29. Other Pre-specified Outcome

Title	Change From Baseline in Bicarbonate (HCO3) at Week 6 (Acute Phase)
▼ Description	Change from baseline to acute phase endpoint in laboratory assessment for bicarbonate, HCO3.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	110	116
Mean (Standard Deviation)		

Unit of Measure: milliEq/Liter		
Baseline	22.43 (3.01)	23.23 (2.81)
Change to Last Observation	2.08 (2.91)	1.38 (2.97)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.047
	Comments	P-value is for treatment comparison of change from baseline on Bicarbonate, HCO3. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANOVA
	Comments	Model: Rank-transformed change from Baseline = Treatment + Investigator.

30. Other Pre-specified Outcome

Title	Change From Baseline in Creatinine at Week 6 (Acute Phase)
▼ Description	Change from baseline to acute phase endpoint in laboratory assessment of creatinine.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	109	116
Mean (Standard Deviation) Unit of Measure: milligram/deciliter (mg/dL)		
Baseline	0.79 (0.15)	0.78 (0.17)
Change to Last Observation	-0.00 (0.20)	0.01 (0.09)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.033
	Comments	P-value is for treatment comparison of change from baseline on creatinine. P-values are

	not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
Method	ANOVA
Comments	Model: Rank-transformed change from Baseline = Treatment + Investigator.

31. Other Pre-specified Outcome

Title	Change From Baseline in the Platelet Count at Week 6 (Acute Phase)
▼ Description	Change from baseline to acute phase endpoint in laboratory assessment of platelet count.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	106	113

Mean (Standard Deviation) Unit of Measure: Thousand/microliter		
Baseline	266.92 (77.19)	281.22 (66.78)
Change to Last Observation	-2.20 (43.10)	-11.00 (40.65)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.034
	Comments	P-value is for treatment comparison of change from baseline on platelet count. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANOVA
	Comments	Model: Rank-transformed change from baseline = Treatment + Investigator.

32. Other Pre-specified Outcome

Title	Change From Baseline in Inorganic Phosphorus at Week 6 (Acute Phase)
▼ Description	Change from baseline to acute phase endpoint in laboratory assessment of inorganic phosphorus.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	109	116
Mean (Standard Deviation) Unit of Measure: mg/dL		
Baseline	3.63 (0.60)	3.68 (0.54)
Change to Last Observation	-0.17 (0.50)	0.01 (0.56)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.007
	Comments	P-value is for treatment comparison of change from baseline on inorganic phosphorus. P-values are

	not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
Method	ANOVA
Comments	Model: Rank-transformed change from Baseline = Treatment + Investigator.

33. Other Pre-specified Outcome

Title	Change From Baseline in Uric Acid at Week 6 (Acute Phase)
▼ Description	Change from baseline to acute phase endpoint in laboratory assessment of uric acid.
Time Frame	Baseline, 6 weeks

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants with baseline and at least 1 post-baseline value.

Arm/Group Title	Duloxetine	Placebo
▼ Arm/Group Description:	Participants received 30 milligrams (mg) duloxetine (oral [po], once daily [QD]) for 1 week followed by 5 weeks at 60 mg in the acute placebo-controlled period.	Participants received placebo (po, QD) for 6 weeks (acute phase). If the participant completes the 6-week double-blind portion of the trial, the participant will be offered the option to participate in the open-label extension period (given 60, 90, or 120 mg QD for 12 weeks).
Overall Number of Participants Analyzed	110	116
Mean (Standard Deviation)		

Unit of Measure: mg/dL		
Baseline	5.19 (1.58)	4.74 (1.30)
Change to Last Observation	-0.23 (0.67)	-0.04 (0.60)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine, Placebo
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.025
	Comments	P-value is for treatment comparison of change from baseline on uric acid. P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	ANOVA
	Comments	Model: Rank-transformed change from Baseline = Treatment + Investigator.

34. Other Pre-specified Outcome

Title	Change From Baseline in Monocytes at Week 18 (Open-label Extension Phase)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	198
Mean (Standard Deviation) Unit of Measure: Thousand/microliter	
Baseline	0.38 (0.14)
Change to Last Observation	0.02 (0.14)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.035
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Wilcoxon (Mann-Whitney)
	Comments	Wilcoxon signed rank test of mean change from extension phase baseline to endpoint on monocytes.

35. Other Pre-specified Outcome

Title	Change From Baseline in Sodium at Week 18 (Open-label Extension Phase)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	201
Mean (Standard Deviation) Unit of Measure: milliEq/Liter	
Baseline	140.08 (3.04)
Change to Last Observation	-0.36 (2.76)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.042
	Comments	

	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
Method	Wilcoxon (Mann-Whitney)
Comments	Wilcoxon signed rank test of mean change from extension phase baseline to endpoint on sodium.

36. Other Pre-specified Outcome

Title	Change From Baseline in Total Protein at Week 18 (Open-label Extension Phase)
▼ Description	[Not Specified]
Time Frame	Baseline (6 weeks), Endpoint (18 weeks)

▼ Outcome Measure Data

▼ Analysis Population Description
Number of randomized participants who entered and had at least 1 non-missing value during extension phase.

Arm/Group Title	Duloxetine
▼ Arm/Group Description:	All participants randomized to placebo or duloxetine in the acute phase took duloxetine during extension phase: 60, 90, or 120 mg QD for 12 weeks (open-label extension phase).
Overall Number of Participants Analyzed	202
Mean (Standard Deviation) Unit of Measure: gram/deciliter (g/dL)	
Baseline	7.04 (0.43)
	-0.06 (0.36)

Change to Last Observation	

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Duloxetine
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.036
	Comments	P-values are not adjusted for multiple comparisons. The a priori threshold for statistical significance was 0.05.
	Method	Wilcoxon (Mann-Whitney)
	Comments	Wilcoxon signed rank test of mean change from extension phase baseline to endpoint on total protein.

Adverse Events

Go to

Time Frame	[Not Specified]
Adverse Event Reporting Description	[Not Specified]

Arm/Group Title	Duloxetine - Double-Blind Acute Phase	Placebo - Double-Blind Acute Phase	Dulox Ex
▼ Arm/Group Description	60 mg oral (po), once daily (QD) for 6 weeks (acute phase)	Oral, QD for 6 weeks	Participa receiving placebo

					duloxeti mg QD f label ext

All-Cause Mortality

	Duloxetine - Double-Blind Acute Phase		Placebo - Double-Blind Acute Phase		Duloxe Ext
	Affected / at Risk (%)		Affected / at Risk (%)		Affected /
Total	--/--		--/--		-

Serious Adverse Events

	Duloxetine - Double-Blind Acute Phase		Placebo - Double-Blind Acute Phase		Duloxe Ext
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected /
Total	4/118 (3.39%)		0/121 (0.00%)		7/209
Infections and infestations					
Cystitis †1	1/118 (0.85%)	1	0/121 (0.00%)	0	0/209
Pneumonia †1	0/118 (0.00%)	0	0/121 (0.00%)	0	1/209
Urinary tract infection †1	0/118 (0.00%)	0	0/121 (0.00%)	0	1/209
Wound infection †1	1/118 (0.85%)	1	0/121 (0.00%)	0	0/209
Injury, poisoning and procedural complications					
Muscle strain †1	1/118 (0.85%)	1	0/121 (0.00%)	0	0/209
Musculoskeletal and connective tissue disorders					
Osteoarthritis †1	0/118 (0.00%)	0	0/121 (0.00%)	0	1/209
Nervous system disorders					
	0/118 (0.00%)	0	0/121 (0.00%)	0	2/209

Multiple sclerosis relapse †1					
Psychiatric disorders					
Suicidal ideation †1	0/118 (0.00%)	0	0/121 (0.00%)	0	1/209
Suicide attempt †1	1/118 (0.85%)	1	0/121 (0.00%)	0	0/209
Respiratory, thoracic and mediastinal disorders					
Bronchospasm †1	0/118 (0.00%)	0	0/121 (0.00%)	0	1/209
Surgical and medical procedures					
Cholecystectomy †1	0/118 (0.00%)	0	0/121 (0.00%)	0	1/209

† Indicates events were collected by systematic assessment

1 Term from vocabulary, MedDRA 13.1

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	1%

	Duloxetine - Double-Blind Acute Phase		Placebo - Double-Blind Acute Phase		Duloxe Ext
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected /
Total	70/118 (59.32%)		59/121 (48.76%)		130/209
Cardiac disorders					
Palpitations †1	0/118 (0.00%)	0	2/121 (1.65%)	2	1/209
Eye disorders					
Vision blurred †1	1/118 (0.85%)	1	0/121 (0.00%)	0	4/209
Gastrointestinal disorders					
	3/118 (2.54%)	3	2/121 (1.65%)	2	0/209

Abdominal discomfort [†1]					
Abdominal distension [†1]	0/118 (0.00%)	0	0/121 (0.00%)	0	3/209
Abdominal pain upper [†1]	2/118 (1.69%)	2	1/121 (0.83%)	1	1/209
Constipation [†1]	7/118 (5.93%)	7	5/121 (4.13%)	5	3/209
Diarrhoea [†1]	5/118 (4.24%)	5	2/121 (1.65%)	2	7/209
Dry mouth [†1]	7/118 (5.93%)	7	3/121 (2.48%)	3	5/209
Nausea [†1]	9/118 (7.63%)	10	7/121 (5.79%)	7	9/209
Vomiting [†1]	3/118 (2.54%)	3	0/121 (0.00%)	0	5/209
General disorders					
Fatigue [†1]	9/118 (7.63%)	9	7/121 (5.79%)	7	14/209
Feeling jittery [†1]	1/118 (0.85%)	1	2/121 (1.65%)	2	0/209
Oedema peripheral [†1]	1/118 (0.85%)	1	0/121 (0.00%)	0	5/209
Pyrexia [†1]	0/118 (0.00%)	0	3/121 (2.48%)	3	1/209
Infections and infestations					
Bronchitis [†1]	0/118 (0.00%)	0	3/121 (2.48%)	3	1/209
Gastroenteritis viral [†1]	2/118 (1.69%)	2	0/121 (0.00%)	0	4/209
Influenza [†1]	2/118 (1.69%)	2	0/121 (0.00%)	0	2/209
Nasopharyngitis [†1]	1/118 (0.85%)	1	2/121 (1.65%)	2	5/209
Sinusitis [†1]	0/118 (0.00%)	0	2/121 (1.65%)	2	4/209
Upper respiratory tract infection [†1]	3/118 (2.54%)	3	2/121 (1.65%)	2	6/209
Urinary tract infection [†1]	1/118 (0.85%)	1	3/121 (2.48%)	3	6/209
Injury, poisoning and procedural complications					
Contusion [†1]	0/118 (0.00%)	0	1/121 (0.83%)	1	3/209
Fall [†1]	2/118 (1.69%)	3	1/121 (0.83%)	1	7/209

Heart rate increased [†1]	0/118 (0.00%)	0	0/121 (0.00%)	0	4/209
Weight decreased [†1]	4/118 (3.39%)	4	0/121 (0.00%)	0	1/209
Weight increased [†1]	1/118 (0.85%)	1	1/121 (0.83%)	1	3/209
Metabolism and nutrition disorders					
Decreased appetite [†1]	7/118 (5.93%)	7	0/121 (0.00%)	0	3/209
Musculoskeletal and connective tissue disorders					
Arthralgia [†1]	1/118 (0.85%)	1	0/121 (0.00%)	0	6/209
Back pain [†1]	1/118 (0.85%)	1	2/121 (1.65%)	2	3/209
Musculoskeletal pain [†1]	1/118 (0.85%)	1	0/121 (0.00%)	0	3/209
Pain in extremity [†1]	4/118 (3.39%)	5	1/121 (0.83%)	1	4/209
Sensation of heaviness [†1]	0/118 (0.00%)	0	1/121 (0.83%)	1	3/209
Nervous system disorders					
Balance disorder [†1]	4/118 (3.39%)	4	2/121 (1.65%)	2	1/209
Dizziness [†1]	9/118 (7.63%)	10	5/121 (4.13%)	5	4/209
Headache [†1]	5/118 (4.24%)	5	6/121 (4.96%)	6	7/209
Multiple sclerosis relapse [†1]	0/118 (0.00%)	0	2/121 (1.65%)	2	6/209
Paraesthesia [†1]	0/118 (0.00%)	0	1/121 (0.83%)	1	4/209
Somnolence [†1]	6/118 (5.08%)	6	3/121 (2.48%)	3	6/209
Tremor [†1]	1/118 (0.85%)	2	0/121 (0.00%)	0	3/209
Psychiatric disorders					
Anxiety [†1]	1/118 (0.85%)	1	0/121 (0.00%)	0	3/209
Depression [†1]	1/118 (0.85%)	1	2/121 (1.65%)	2	0/209
Insomnia [†1]	4/118 (3.39%)	4	1/121 (0.83%)	1	4/209

Libido decreased †1	3/118 (2.54%)	3	3/121 (2.48%)	3	1/209
Thinking abnormal †1	2/118 (1.69%)	2	0/121 (0.00%)	0	0/209
Respiratory, thoracic and mediastinal disorders					
Cough †1	0/118 (0.00%)	0	0/121 (0.00%)	0	3/209
Oropharyngeal pain †1	0/118 (0.00%)	0	2/121 (1.65%)	2	2/209
Skin and subcutaneous tissue disorders					
Ecchymosis †1	2/118 (1.69%)	3	0/121 (0.00%)	0	0/209
Hyperhidrosis †1	2/118 (1.69%)	2	0/121 (0.00%)	0	3/209
Vascular disorders					
Hypertension †1	1/118 (0.85%)	1	2/121 (1.65%)	2	1/209

† Indicates events were collected by systematic assessment

1 Term from vocabulary, MedDRA 13.1

Limitations and Caveats

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[Not Specified]

More Information

Go to

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact

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Phone:	800-545-5979
Responsible Party:	Eli Lilly and Company
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