Sexual Functioning Assessed in 4 Double-Blind Placebo- and Paroxetine-Controlled Trials of Duloxetine for Major Depressive Disorder

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Objective: The onset or worsening of sexual dysfunction is a common treatment-emergent side effect of antidepressant medications. Post hoc analyses of pooled data from placebo-controlled studies were utilized to assess sexual functioning in patients receiving duloxetine or paroxetine.

Method: Acute-phase data were obtained from four 8-week, double-blind, placebo- and paroxetine-controlled trials of similar design in which patients meeting DSM-IV criteria for major depressive disorder were randomly assigned to receive placebo (N = 371), duloxetine (40–120 mg/day; N = 736), or paroxetine (20 mg/day; N = 359). Pooling of data from these studies was anticipated during study design. This represented all available data from duloxetine studies in which the Arizona Sexual Experience Scale (ASEX) was administered both at baseline and endpoint. Long-term data were available from extension phases in 2 of these trials in which acute treatment responders received placebo (N = 129), duloxetine (80–120 mg/day; N = 297), or paroxetine (20 mg/day; N = 140) for an additional 26 weeks. Data were collected between March 2000 and July 2002.

Results: The incidence of acute treatment-emergent sexual dysfunction was significantly lower among duloxetine-treated patients compared with those receiving paroxetine ($p = .015$), although both rates were significantly higher than placebo ($p = .007$ and $p < .001$ for duloxetine and paroxetine, respectively). Treatment group differences in the incidence of treatment-emergent dysfunction did not vary significantly by gender. In female patients, acute treatment-emergent sexual dysfunction was significantly lower in the duloxetine treatment group compared with the paroxetine treatment group ($p = .032$), with both rates being significantly higher than placebo ($p = .049$ and $p < .001$ for duloxetine and paroxetine, respectively). In the somewhat smaller group of male patients, acute treatment-emergent dysfunction did not differ significantly between duloxetine and placebo treatment groups, but the incidence was significantly higher in paroxetine-treated male patients compared with male placebo patients ($p = .012$). The long-term incidence of treatment-emergent dysfunction did not differ significantly between duloxetine-, paroxetine-, and placebo-treated patients.

Conclusion: In this analysis of pooled data, patients receiving duloxetine (40–120 mg/day) or paroxetine (20 mg/day) had a significantly higher incidence of acute treatment-emergent sexual dysfunction when compared with placebo patients. However, the incidence of acute treatment-emergent dysfunction for duloxetine was significantly lower than that observed for paroxetine.

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Sexual dysfunction is highly prevalent both in the general population and, to an even greater extent, in patients with major depressive disorder (MDD). In the general population, 43% of women and 31% of men report problems with sexual functioning.[1] In depressed patients, the prevalence of dysfunction has consistently been shown to be higher than that in healthy controls.[2–4] Up to 70% of depressed patients experience problems with sexual functioning, with decreased libido being the most common complaint.[5,6] Furthermore, erectile dysfunction is reported to be twice as common in depressed men as in nondepressed controls.[7]

The onset or worsening of sexual dysfunction is also frequently encountered as a treatment-emergent side effect

associated with antidepressant therapy.[8,9] The emergence of sexual dysfunction during antidepressant treatment is an important contributor to treatment noncompliance[10] and can impair quality of life.[11] However, the high rates of baseline sexual dysfunction among depressed patients greatly complicate the assessment of changes in sexual functioning during antidepressant therapy.[5,12] Medications with predominantly serotonergic effects have generally been associated with the highest incidence of treatment-emergent sexual dysfunction. The incidence of dysfunction in depressed patients undergoing therapy with selective serotonin reuptake inhibitors (SSRIs) has been reported to be as high as 73%.[9,13,14]

Some antidepressants have consistently been associated with a lower incidence of sexual dysfunction, most notably nefazodone, bupropion, and mirtazapine. The pharmacologic profiles of these medications appear to be consistent with the observed low rates of sexual dysfunction. Nefazodone potently and selectively blocks postsynaptic serotonin 5-HT_{2A} receptors and is a weak inhibitor of serotonin (5-HT) and norepinephrine (NE) reuptake.[15] Bupropion may enhance neurotransmission of dopamine (DA) and NE while possessing essentially no serotonergic properties.[16] Mirtazapine increases noradrenergic neurotransmission through blockade of presynaptic central α_2-adrenergic autoreceptors, in addition to its blockade of inhibitory α_2-heteroreceptors located on serotonergic neurons.[17]

Duloxetine is a potent and relatively balanced dual reuptake inhibitor of 5-HT and NE, which lacks significant affinity for muscarinic, histamine$_1$, α_1-adrenergic, and opioid receptors.[18] In healthy human subjects, duloxetine (80–120 mg/day) decreases urinary excretion of NE metabolites similar in magnitude to desipramine 100 mg, providing in vivo evidence of NE uptake inhibition.[19] The efficacy of duloxetine in the treatment of MDD has been established in randomized, double-blind, placebo-controlled studies.[20–24] We wished to investigate changes in sexual functioning in depressed patients treated with duloxetine and to compare these effects with those observed in patients receiving the SSRI paroxetine.

Assessment of treatment-emergent sexual dysfunction can be problematic. Patients are often unwilling or embarrassed to report adverse events related to sexual functioning, leading to a pronounced underestimation of the incidence of such events in clinical trials.[5] One study of SSRI-induced sexual dysfunction found an incidence of 58% when patients were directly questioned, as opposed to 14% when dysfunction was assessed using spontaneously reported adverse events.[13] Therefore, the use of a validated questionnaire that solicits specific information related to sexual functioning is widely viewed as a superior approach to the assessment of treatment-emergent sexual dysfunction.[11,25] In the present analysis, the Arizona Sexual Experience Scale (ASEX), a validated scale of elicited sexual function,[26] was utilized to assess changes in sexual functioning associated with duloxetine during the treatment of MDD.

METHOD

Data

Sexual functioning was assessed in 4 double-blind, placebo- and paroxetine-controlled studies of duloxetine (40–120 mg/day) for the treatment of MDD. This represented all available data from studies in which the ASEX scale was administered at both baseline and endpoint. The 4 studies involved 2 separate protocols, with each protocol including 2 independent, but identical studies. These 4 studies were prospectively designed to be sufficiently similar as to allow pooling of data for safety analyses in order to meet expectations of regulatory agencies for new drug applications. The primary efficacy outcome in each study was mean change from baseline in the 17-item Hamilton Rating Scale for Depression (HAM-D-17)[27] total score. A summary of results from study 1[28] is available online through Eli Lilly and Company, Indianapolis, Ind. Efficacy and safety data from studies 2,[24] 3,[29] and 4[30] have been published or presented previously. Data were collected between March 2000 and July 2002.

All 4 studies were conducted in a double-blind fashion to minimize bias in the ratings of efficacy or tolerability associated with the onset and conclusion of therapy. All 4 studies featured an 8-week acute treatment phase in which patients meeting DSM-IV criteria for MDD were randomly assigned to receive placebo, 1 of 2 doses of duloxetine, or paroxetine (20 mg q.d.). In studies 1 and 2, the duloxetine dose was either 40 mg/day (20 mg b.i.d.) or 80 mg/day (40 mg b.i.d.), while in studies 3 and 4, the duloxetine dose was either 80 mg/day (40 mg b.i.d.) or 120 mg/day (60 mg b.i.d.). In studies 3 and 4, patients having a ≥ 30% decrease in HAM-D-17 total score from baseline during acute treatment were eligible to enter an extension phase and were allowed to continue the same treatment for an additional 26 weeks. All protocols were approved by the ethics committee at each site in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent prior to the administration of any study procedures or study drug.

The term *acute phase data* refers to pooled data from the 8-week acute phases of studies 1 to 4. The terms *long-term data* or *acute and continuation phase data* refer to pooled data from the acute and extension phases of studies 3 and 4. Throughout the "Results" section, the term *sexual dysfunction* is used to indicate that a patient or group of patients met ASEX criteria[26] for sexual dysfunction.

ASEX

The ASEX was utilized in all 4 studies to assess sexual function. The ASEX, developed by McGahuey et al.,[26] is a patient-rated scale comprising 5 questions, with responses

measured on a 6-point Likert scale. Therefore, the total score can vary from a minimum of 5 to a maximum score of 30. The questions are the same for male and female patients, except for question 3. The questions on the scale are as follows:

1. How strong is your sex drive?
2. How easily are you sexually aroused (turned on)?

Female
3. How easily does your vagina become moist or wet during sex?

Male
3. Can you easily get and keep an erection?

4. How easily can you reach an orgasm?
5. Are your orgasms satisfying?

Questions 3 to 5 are answered only if the patient has been sexually active in the past month.

The following criteria were used to categorize a patient as having clinically relevant sexual dysfunction:

- an ASEX total score of 19 or greater, or
- a score of 5 or greater on any item, or
- a score of 4 or greater on any 3 items

In studies 1 and 2, the ASEX was administered prior to randomization (baseline) and at weeks 6 and 8, or at the visit at which a patient discontinued from the trial. In studies 3 and 4, the ASEX was administered prior to randomization (baseline) and at weeks 8 and 34 (extension phase patients), or at the visit at which a patient discontinued from the trial.

Statistical Analyses

All patients who completed at least questions 1 and 2 of the ASEX at baseline and at least 1 postbaseline visit were included in the analyses. Patients were categorized as having or not having sexual dysfunction based on whether they met ASEX criteria for sexual dysfunction as previously described.[26] In analyses of individual ASEX questions, dysfunction was defined as a score ≥ 5.

The primary analytic approach assessed the incidence of sexual dysfunction, as defined by ASEX criteria,[26] using logistic regression with a model that included protocol, baseline category, treatment, baseline category by treatment interaction, and baseline score (sum of questions 1 and 2). *Baseline category* refers to the presence or absence of sexual dysfunction at baseline. By including this term and its interaction with treatment, all patients were included in the analyses, but inferences could be made separately for those patients with and without dysfunction at baseline. A similar approach was used to assess results by gender. Specifically, the main effect of gender and its interactions with other terms in the primary analytic model were added so that all patients could be included in the analyses, but inferences could be drawn separately for male and female patients.

Analyses of the incidence and resolution of sexual dysfunction were replicated after adjustment for endpoint HAM-D-17 total score (i.e., by adding change to endpoint in HAM-D-17 total score as a covariate to the previously described analyses, all treatment groups were adjusted to show an equal baseline-to-endpoint improvement in depressive symptoms). Adjusting for differential improvements in depression allowed an evaluation of drug effects on sexual functioning independent of the effects the drugs may have on depression. Such a comparison is important because treatment differences in sexual functioning could be an indirect effect due to differential responses in depression rather than a direct effect on sexual functioning.

Since the current study focused on a safety-related topic (antidepressant-induced sexual dysfunction), our objective was to present analyses that highlighted any drug-placebo differences. In this regard, the most appropriate approach was one in which a correction for multiple comparisons (e.g., Bonferroni) was not employed. If a Bonferroni or similar correction were to be implemented, statistical power would be lost, and the ability to detect causal drug effects would be greatly diminished. Omitting an adjustment for multiplicity is the standard analytic approach when evaluating safety and tolerability of drugs for regulatory purposes. However, results should be interpreted in light of this approach and the possibility for type I errors to exist.

RESULTS

Patient Characteristics

A total of 1466 patients were randomly assigned in the 4 studies. The numbers of patients within each individual study are presented in Table 1. Treatment groups did not differ significantly by age, gender, or origin within any of the studies. The mean ages of patients ranged from 40.5 to 45.2 years within the 4 trials. Of the 1466 randomly assigned patients, 1345 patients provided responses to ASEX questions 1 and 2. Questions 3, 4, and 5 were to be answered only if the patient had been sexually active in the past month—a total of 833 patients answered all 5 ASEX questions.

A total of 870 patients (59.3%) met ASEX criteria[26] for sexual dysfunction at baseline within the acute phase database, with a point prevalence of 635/975 (65.1%) for women and 235/491 (47.9%) for men. In the long-term database, 513 patients (67.6%) met criteria for dysfunction at baseline (i.e., at entry into the acute phase).

Acute Phase Treatment-Emergent Dysfunction

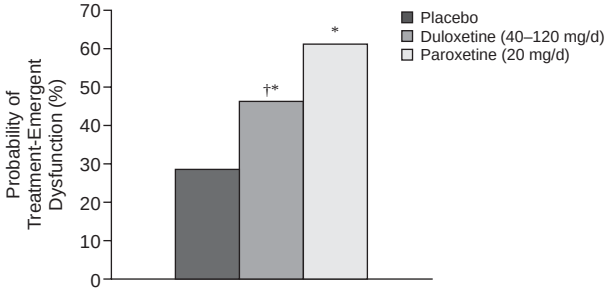
In the 475 patients who did not meet ASEX criteria for sexual dysfunction at baseline (duloxetine, N = 241;

Table 1. Details of Four 8-Week, Double-Blind, Placebo- and Paroxetine-Controlled Studies of Duloxetine for Patients With Major Depressive Disorder[a]

		Number of Patients				
			Duloxetine			
Study	Duration, wk	Placebo	(40 mg/d)[b]	(80 mg/d)[c]	(120 mg/d)[d]	Paroxetine[e]
1	8	90	91	84	0	89
2	8	89	86	91	0	87
3	8	93	0	95	93	86
	(+26)	(58)		(70)	(75)	(70)
4	8	99	0	93	103	97
	(+26)	(71)		(71)	(81)	(70)
Total (acute phase)		371		736		359
Total (long term)		129		297		140

[a]Long-term data were available from extension phases in studies 3 and 4.
[b]Administered 20 mg b.i.d.
[c]Administered 40 mg b.i.d.
[d]Administered 60 mg b.i.d.
[e]Administered 20 mg q.d.

Figure 1. Incidence of Acute Treatment-Emergent Sexual Dysfunction in Patients Receiving Placebo, Duloxetine, or Paroxetine.[a]



[a]Numbers of patients providing both baseline and endpoint data for the acute treatment phase: placebo (N = 127 of 371 subjects), duloxetine (40–120 mg/day; N = 241 of 736 subjects), paroxetine (20 mg/day; N = 107 of 359 subjects).
*p < .01 vs. placebo.
†p = .015 vs. paroxetine.

paroxetine, N = 107; placebo, N = 127), the incidence of treatment-emergent dysfunction for duloxetine or paroxetine was significantly higher than that observed for placebo (duloxetine 46.4% vs. placebo 28.8%; t = 2.69, df = 1337, p = .007; paroxetine 61.4% vs. placebo 28.8%; t = 4.30, df = 1337, p < .001; Figure 1). The incidence of dysfunction in patients receiving duloxetine was significantly lower than that for paroxetine-treated patients (t = –2.43, df = 1337, p = .015) during acute treatment (Figure 1). Relative risks for acute-phase treatment-emergent dysfunction (vs. placebo) were 1.6 for duloxetine and 2.1 for paroxetine.

In female patients, the incidence of dysfunction for both duloxetine and paroxetine was significantly higher than that for placebo (duloxetine: t = 1.97, df = 1331, p = .049; paroxetine: t = 3.47, df = 1331, p < .001; Figure 2A). The incidence of acute treatment-emergent dysfunction was significantly lower among female patients receiving duloxetine compared with female patients receiving paroxetine (t = –2.15, df = 1331, p = .032). In male patients, the acute-phase incidence of treatment-emergent dysfunction was significantly higher for paroxetine compared with placebo (t = 2.53, df = 1331, p = .012; Figure 2B). Incidence of dysfunction among duloxetine-treated male patients did not differ significantly from male placebo patients but was similar in magnitude to that observed in duloxetine-treated female patients.

The incidence of acute treatment-emergent dysfunction was analyzed for each individual ASEX item, where a score of ≥ 5 was used to define dysfunction.[26] For the ASEX item assessing "ease of orgasm," the incidence of dysfunction was significantly higher in duloxetine- and paroxetine-treated patients compared with placebo patients (duloxetine 16.4% vs. placebo 8.6%; t = 2.27, df = 827, p = .024; paroxetine 19.6% vs. placebo 8.6%; t = 2.70, df = 827, p = .007, respectively). No other significant differences existed between the 3 treatment groups on individual ASEX items.

In male patients receiving duloxetine or paroxetine, the incidence of acute-phase dysfunction on the ASEX item assessing "ease of orgasm" was significantly higher than in male placebo patients (duloxetine 17.8% vs. placebo 6.4%; t = 2.13, df = 821, p = .033; paroxetine 25.1% vs. placebo 6.4%; t = 2.85, df = 821, p = .005). Duloxetine-treated male patients also exhibited significantly higher acute phase incidence of dysfunction compared with male placebo patients in the assessment of "satisfaction from orgasm" (duloxetine 12.2% vs. placebo 1.5%; t = 2.29, df = 820, p = .022). In female patients, the incidence of dysfunction did not differ between treatment groups for any individual ASEX item.

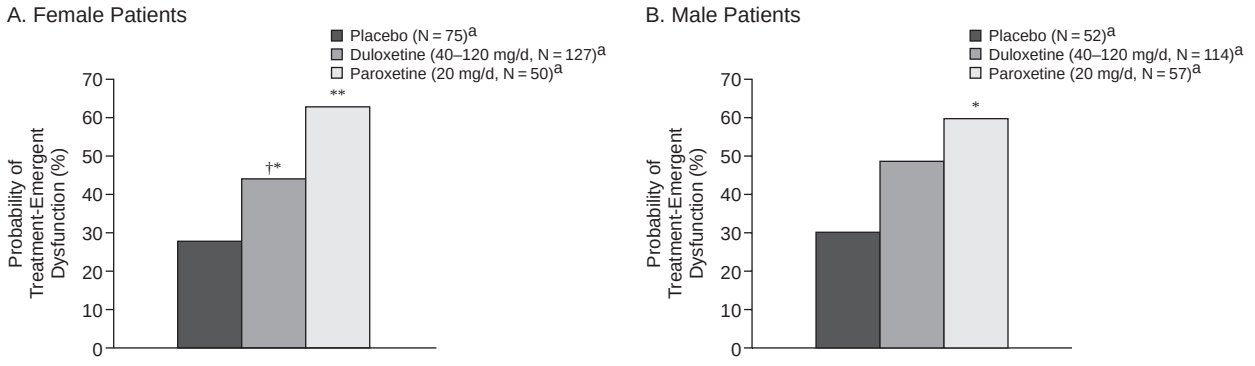
Acute Phase Resolution of Dysfunction

In the 870 patients with sexual dysfunction at baseline, there were no significant between-group differences in the incidence of resolution of dysfunction during acute-phase treatment (duloxetine 34.9%, paroxetine 36.1%, placebo 29.9%). Similarly, when the incidence of resolution of dysfunction was analyzed by gender, or by individual ASEX question, there were no significant differences in the probability of regaining normal functioning during acute-phase treatment with duloxetine, paroxetine, or placebo.

Long-Term Treatment-Emergent Dysfunction

There were no significant differences between the 3 treatment groups in the long-term incidence of treatment-emergent dysfunction (duloxetine 39.4%, paroxetine 45.5%, placebo 35.3%).

Figure 2. Incidence of Acute Treatment-Emergent Sexual Dysfunction in Patients Receiving Placebo, Duloxetine, or Paroxetine



[a]Figures in parentheses are the total numbers of patients providing both baseline and endpoint data for each treatment phase.
*p < .05 vs. placebo.
**p < .001 vs. placebo.
†p < .05 vs. paroxetine.

Long-Term Resolution of Dysfunction

In those patients with sexual dysfunction at baseline (i.e., at the start of the acute phase), there were no significant between-group differences in the incidence of resolution of dysfunction during 34 weeks of treatment (duloxetine 43.3%, paroxetine 47.4%, placebo 34.7%).

Of those patients who had sexual dysfunction at the conclusion of acute-phase treatment, between-group differences in the incidence of resolution of dysfunction were not statistically significant.

Adjustment for Changes in Depression

Results obtained after accounting for endpoint changes in depression were similar to the unadjusted results. Thus, the incidence of acute-phase treatment-emergent dysfunction for duloxetine (45.7%) was significantly lower than that for paroxetine (63.8%, $t = -2.87$, $df = 1332$, $p = .004$). The incidence of dysfunction for both duloxetine and paroxetine was significantly higher than that for placebo (24.8%, $t = 3.21$, $df = 1332$, $p = .001$ vs. duloxetine; $t = 5.07$, $df = 1332$, $p < .001$ vs. paroxetine).

No significant differences were found between the 3 treatment groups in the long-term incidence of treatment-emergent dysfunction following adjustment for endpoint HAM-D-17 total score (duloxetine 39.5%, paroxetine 46.3%, placebo 27.1%).

No significant between-group differences were found in the incidence of resolution of dysfunction during acute-phase or long-term treatment (acute-phase: duloxetine 32.6%, paroxetine 34.2%, placebo 31.4%; long-term: duloxetine 39.7%, paroxetine 42.2%, placebo 37.5%).

Discontinuation Due to Adverse Events

The overall rate of discontinuation due to any spontaneously reported adverse event in acute-phase studies was 8.6% for duloxetine-treated patients compared with 7.0% for paroxetine-treated patients ($p = .408$). Two of the events leading to discontinuation were related to sexual functioning. Discontinuations due to these events did not differ significantly between treatment groups (erectile dysfunction: duloxetine 1.2% vs. paroxetine 0.8%; anorgasmia: duloxetine 0.1% vs. paroxetine 0.3%). During the 26-week continuation phase, no patients discontinued due to adverse events related to sexual functioning.

DISCUSSION

In these pooled analyses, the incidence of acute treatment-emergent sexual dysfunction in patients receiving duloxetine (40–120 mg/day) was found to be significantly lower than that in patients receiving paroxetine (20 mg/day), although the incidence in the active treatment groups was significantly higher than that in the placebo group. The relative rates of dysfunction in female patients receiving duloxetine, paroxetine, or placebo were similar to those observed in male patients. During long-term treatment (34 weeks), the incidence of treatment-emergent sexual dysfunction did not differ significantly between duloxetine, paroxetine, and placebo treatment groups.

The results of the present investigation provide initial insight into changes in sexual functioning among depressed patients receiving duloxetine treatment for up to 34 weeks. Given that both depressive illness and antidepressant treatment can produce changes in sexual functioning, a complete assessment of the "true" incidence of antidepressant-induced dysfunction is beyond the scope of the current post hoc analyses. However, the results presented here were derived from a validated, patient-rated measure of sexual functioning and are expected to yield a far more accurate assessment of duloxetine-induced

sexual dysfunction than that obtained from spontaneous reporting of treatment-emergent adverse events.

The high prevalence of sexual dysfunction in untreated depressed patients is well documented.[2,4,5] In a recent survey of 4557 patients with MDD,[6] the prevalence of sexual dysfunction in untreated patients was 65%. Results from the current analyses are consistent with this observation. Within the acute phase database, 59% of patients met ASEX criteria[26] for sexual dysfunction at baseline, while, in the acute and continuation phase database, the baseline prevalence was 68%. These high rates of baseline sexual dysfunction often complicate the assessment of treatment-emergent dysfunction during subsequent antidepressant therapy.[5,12] To avoid the confounding effects of preexisting dysfunction, the current analyses focused upon the incidence of dysfunction in the subset of patients who reported normal sexual functioning at baseline.

Widely varying estimates of the incidence of sexual dysfunction associated with antidepressant therapy arise not only from the differences in pharmacology between classes of medication, but also from the lack of a standardized definition of sexual dysfunction and differing methodologies used to collect sexual functioning data. For example, Clayton et al.[25] utilized the Changes in Sexual Functioning Questionnaire (CSFQ) to assess the prevalence of sexual dysfunction in 6297 patients receiving antidepressant monotherapy and found an overall rate of dysfunction of 37% (range, 22%–43% across the studied medications). However, these data were obtained using a threshold CSFQ total score to define dysfunction and reflect the proportion of patients with global sexual dysfunction. In contrast, ASEX criteria allow for inclusion of patients who have a score ≥ 5 on only 1 item, indicating that dysfunction affects only 1 phase of the sexual response cycle. Furthermore, the Clayton et al. study[25] did not assess sexual functioning at baseline, and, therefore, the reported prevalence of dysfunction during therapy may have included patients who had preexisting dysfunction.

Treatment-emergent changes in sexual functioning during antidepressant treatment may differ substantially in male and female patients.[31] Studies involving SSRI and SNRI (serotonin-norepinephrine reuptake inhibitor) treatment of depressed patients have found significantly greater impairment of sexual drive and desire in men compared with women,[32] in addition to a higher incidence of orgasmic dysfunction in male patients.[31–33] In the current analysis of ASEX individual items, a similar pattern of gender differences was observed. Among female patients receiving duloxetine or paroxetine, the incidence of acute treatment-emergent dysfunction did not differ significantly from that in female placebo patients on any of the 5 ASEX items. In male patients, the incidence of acute treatment-emergent dysfunction was significantly higher for duloxetine and paroxetine compared with placebo on the item assessing ease of orgasm. Furthermore, duloxetine-treated male patients had a significantly higher incidence of dysfunction on the item assessing satisfaction from orgasm when compared with male placebo patients.

In previous studies, it has been reported that patients who experience worsening in sexual functioning in the early stages of antidepressant therapy may improve over longer periods of observation.[34] In the present analysis, patients receiving duloxetine or paroxetine had a long-term incidence of dysfunction that was substantially lower than that observed during acute-phase treatment. If the difference in the incidence of dysfunction between drug and placebo is utilized as a measure of "true" antidepressant-induced dysfunction, these differences declined markedly from the acute phase to long-term treatment. The decline in the rate of dysfunction during long-term antidepressant treatment may be driven by the concurrent improvement in depressive symptoms,[35,36] an effect that appears to be more prominent during long-term therapy. However, additional studies will be required to fully characterize the interrelationship between improvement in depressive symptoms and long-term resolution of sexual dysfunction.

The results of the present analysis should be considered in light of several limitations:

1. These were post hoc analyses of pooled data from 4 clinical trials of duloxetine.
2. None of the studies employed the recommended therapeutic duloxetine dose of 60 mg once daily.
3. Only 2 of the studies featured extension phases, resulting in a long-term study population that was substantially smaller than the acute-phase population. Furthermore, long-term data were obtained only from patients within these 2 studies who met predefined response criteria to enter the extension phase.
4. The SSRI comparator in this study, paroxetine, has been associated with somewhat higher reported rates of associated sexual dysfunction than other SSRI medications. Therefore, the current results for duloxetine relative to paroxetine cannot be extrapolated to other SSRIs or to the class as a whole.
5. The ASEX has received only limited use as a research tool,[37–41] and, therefore, a degree of caution should be employed when comparing the results from these analyses with those obtained using other assessment measures.
6. The ASEX was administered only 3 times during the 34-week duration of the long-term studies, which prevented a detailed analysis of the longitudinal course of onset and resolution of sexual dysfunction.

In conclusion, results from the present analysis of pooled data show that patients receiving duloxetine (40–120 mg/day) or paroxetine (20 mg/day) have a significantly higher incidence of acute treatment-emergent

sexual dysfunction when compared with placebo patients. However, the incidence of acute treatment-emergent dysfunction among duloxetine-treated patients was significantly lower than that observed in patients receiving paroxetine. Future prospectively designed studies are warranted.

Drug names: bupropion (Wellbutrin and others), desipramine (Norpramin and others), duloxetine (Cymbalta), mirtazapine (Remeron and others), nefazodone (Serzone and others), paroxetine (Paxil and others).

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