

Safety and Efficacy of Lamotrigine for Adult Bipolar Disorder Patients

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ABSTRACT

Objective

To assess the effectiveness and safety of lamotrigine in the treatment of bipolar disorder.

Methods

Chart reviews of 587 adult outpatients with DSM-IV bipolar disorder and treated with lamotrigine were conducted (mean age 37.6 ± 11.7 years; 72% female; 54.9% bipolar I, 28.3% bipolar II, 16.9% bipolar not otherwise specified). Charts of subjects who received lamotrigine in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and May 2004 were reviewed. Treatment response was assessed with the Clinical Global Impression-Improvement (CGI-I) scale (1 = very marked improvement, 2 = moderate improvement). Relapse was defined as a mood change that occurs 4 weeks after initiation of medication or the return of symptoms from the original episode.

Results

Three hundred fifty-seven subjects (60.8%) taking lamotrigine had marked to moderate improvement (CGI-I scores: 1, 21.1%; 2, 39.7%). Two hundred nineteen subjects (37.3%) relapsed during lamotrigine treatment (mean time to relapse = 207 days). The final mean lamotrigine dose was 120.4 ± 94.3 mg/d. Rash (12.8%) and headache (2.9%) were the most frequently reported side effects.

Conclusion

Lamotrigine appears effective in the treatment of bipolar disorder and was well tolerated.

INTRODUCTION

- Lamotrigine is indicated for the maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes in patients who received standard therapy to treat an acute mood episode.¹
- In large, controlled, double-blind trials, lamotrigine has demonstrated antidepressant efficacy² and has been shown to prolong the time to relapse to a depressive episode³⁻⁵ in patients with bipolar I disorder.
- In patients with bipolar II disorder, lamotrigine has been shown to reduce the risk of relapse over 6 months of monotherapy⁶ and improve depressive symptoms.⁷
- The objective of this study was to assess the effectiveness and safety of lamotrigine in the treatment of bipolar disorder.

METHODS

- This is a retrospective chart review of 587 adult outpatients with DSM-IV bipolar disorder who received treatment with lamotrigine.
- Charts of subjects who received lamotrigine in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and May 2004 were reviewed.
- Charts were reviewed for relapse, adverse events, scores on the Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scales, and lamotrigine dosages.
- Treatment response was assessed with the CGI-I scale (1 = marked improvement, 2 = moderate improvement). Subjects were considered to have responded to therapy if they achieved a CGI-I score of ≤3. Subjects were considered to have relapsed if they experienced a mood change 4 weeks after initiation of medication or a return of symptoms from the original episode.

RESULTS

- Of the 587 subjects reviewed in this study, 72.2% were female, and the mean age was 37.6 years (range 18-79 years). The final mean lamotrigine dose ± SD was 120.4 ± 94.4 mg/day (Table 1).
- 54.9% of subjects were diagnosed with bipolar I disorder, 28.3% with bipolar II disorder, and 16.9% with bipolar disorder not otherwise specified (Figure 1).
- 352 subjects (59.9%) taking lamotrigine had marked-to-moderate improvement, with a CGI-I score of 1 observed in 20.6% of subjects and a CGI-I score of 2 in 39.3%.
- 479 subjects (81.6%) responded to lamotrigine.
- Of the responders, 52% did not relapse, and 29.3% relapsed. The mean time to relapse was 207.0 ± 308.9 days (range 3-1582 days) (Figure 2).
- Within each bipolar disorder type, almost all of patients' CGI-S scores were ≥ 3 at treatment initiation (Figure 3). The majority of subjects with each bipolar subtype had CGI-I scores of 1 or 2 at titration completion (Figure 4).
- The most frequently reported treatment-emergent adverse events were non-serious rash (12.8%) and headache (2.9%) (Table 2).

Table 1. Study Population

Patients	587
Gender (% female)	72
Mean age (y ± SD)	37.6 ± 11.7
Age range (y)	18-79
Final*	120.4 ± 94.4

*Mean lamotrigine dose ± SD (mg/d).

Figure 1. Distribution of Bipolar Subtypes

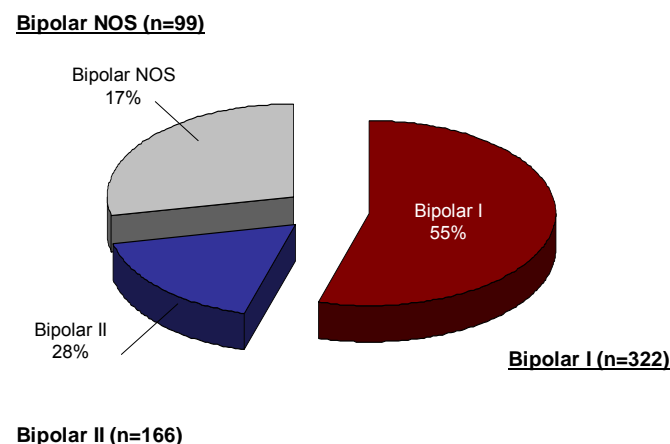
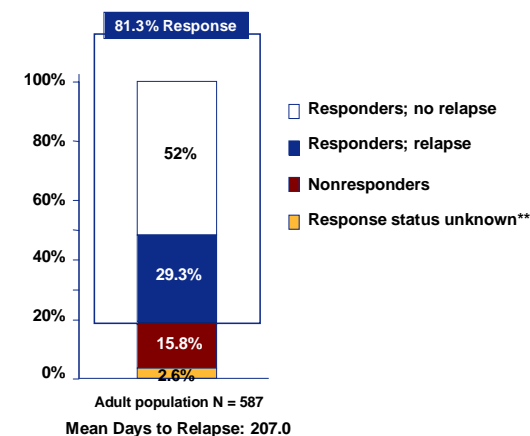


Figure 2. Patient Response and Relapse on Lamotrigine

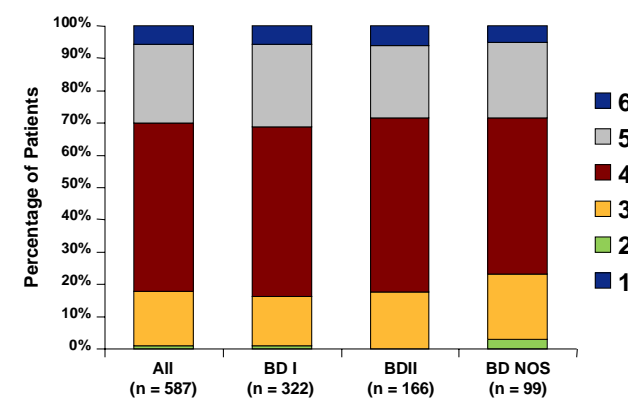


Lamotrigine response is defined as achieving a CGI-I ≤3. Relapse is defined by a change in CGI-I to ≥4 after an observed lamotrigine response, or return of episode.
**Response unknown includes: lost to follow-up, patient discontinued medication prior to assessment.

Table 2. Treatment-Emergent Adverse Events on Lamotrigine

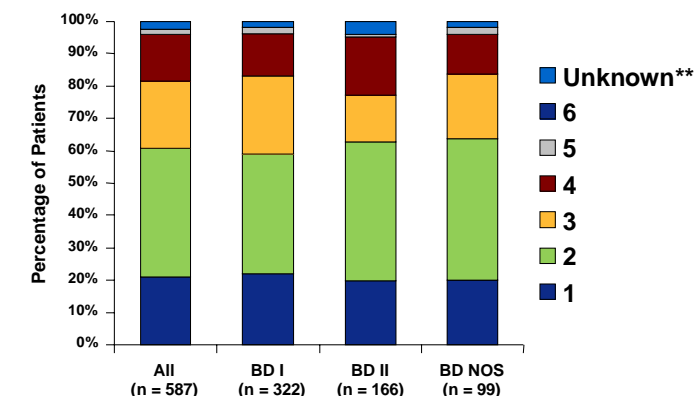
Event	Percentage	Event	Percentage
Non-serious rash	12.8%	Dry mouth	<1%
Headaches	2.9%	Rhinitis	<1%
Nausea	1.7%	Pharyngitis	<1%
Insomnia	1.7%	Exacerbation of cough	<1%
Somnolence	<1%	Constipation	<1%
Back pain	<1%	Abdominal pain	<1%
Vomiting	<1%	Fatigue	<1%
Diarrhea	<1%		

Figure 3. Across BD Subtypes, CGI-S Scores Were Mainly 4-6



BD = bipolar disorder; CGI-S = Clinical Global Impression of Severity; NOS = not otherwise specified.

Figure 4. After Lamotrigine Treatment CGI-I Scores Were Mainly 1 and 2



BD = bipolar disorder; CGI-I = Clinical Global Impression of Improvement; NOS = not otherwise specified.
**Patient discontinued medication prior to follow-up.

CONCLUSIONS

- This large, retrospective study demonstrates that lamotrigine appears effective in the treatment of bipolar disorder in adults.
- Lamotrigine was effective across bipolar disorder subtypes.
- Mean dosages of lamotrigine were similar to those seen in previous trials.
- Lamotrigine was well tolerated, with a low incidence of side effects and no evidence of serious rash.
- Based on these data, placebo-controlled studies are warranted.

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