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ABSTRACT

Objective: To assess the efficacy, safety, and tolerability of extended-release carbamazepine capsules (ERC-CBZ; Shire) in treating patients with bipolar disorder

Method: Data on demographics/characteristics, adverse events, and Clinical Global Impression–Severity (CGI-S) and Clinical Global Impression–Improvement (CGI-I) were obtained and analyzed from the charts of 300 ERC-CBZ–treated adult patients who met DSM-IV criteria for bipolar disorder at a single-site private practice. Comparisons in treatment were also evaluated between manic/mixed vs bipolar I depression or bipolar II subtypes.

Results: At initiation of ERC-CBZ treatment, 84% of patients had CGI-S scores of 5 and higher. During therapy (mean ERC-CBZ dose = 581 ± 213 mg/d), clinical response to ERC-CBZ treatment (CGI-I ≤ 3) occurred in 73% of patients. Relapse (subsequent change to CGI-I ≥ 4) was evident in 33% of patients with prior improvement. Somnolence (11%), dizziness (8%), nausea (8%), and rash (5%) were the most common adverse events. No statistically significant differences were found in efficacy and safety between manic/mixed vs bipolar I depression or bipolar II subgroups.

Conclusion: Treatment with ERC-CBZ was effective, safe, and well tolerated in adult patients with bipolar I, II, and not otherwise specified disorders.

EXTENDED-RELEASE CARBAMAZEPINE CAPSULES IN BIPOLAR DISORDER

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INTRODUCTION

- Carbamazepine (CBZ), an anti-convulsant, has long been a therapeutic option for bipolar disorder
- Carbamazepine has been a prescription choice for the treatment of bipolar disorder for nearly 30 years¹
- Extended-release CBZ capsules (ERC-CBZ; Shire) are a recent formulation developed to improve medical adherence by improving dosing convenience and lowering incidence of adverse events by stabilizing serum CBZ levels^{2,3}
- Recent studies have shown ERC-CBZ to be effective in the treatment of bipolar I patients with mixed and manic episodes^{4,7}
- The purpose of this retrospective study was to analyze the efficacy, safety, and tolerability of ERC-CBZ treatment in adult bipolar patients, including those with bipolar I manic/mixed episodes, bipolar I depression, bipolar II disorder, and bipolar not otherwise specified (NOS)

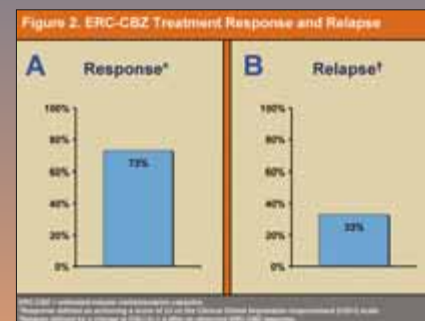
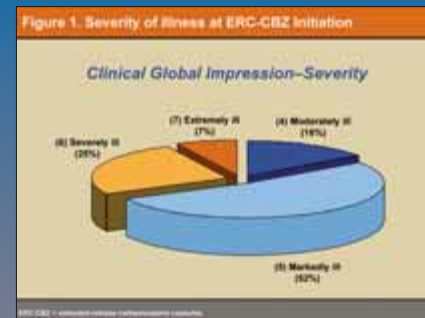
METHODS

- A chart review was conducted at a single-site private practice clinic for 300 ERC-CBZ–treated patients (≥18 years of age) who met DSM-IV criteria for bipolar disorder
- Data obtained included patient demographics, primary and comorbid conditions, dose of ERC-CBZ, concomitant medications, and adverse events
- Clinical Global Impression–Severity (CGI-S) scales were used to assess severity at initiation of ERC-CBZ
- Clinical Global Impression–Improvement (CGI-I) scales were used to assess treatment response
 - Response was defined as a CGI-I no greater than 3
 - Relapse was defined as a CGI-I of at least 4 after a response had been previously observed
- Subanalysis of chart data was conducted to establish the effect of ERC-CBZ therapy on bipolar subpopulations (manic/mixed vs bipolar I depression or bipolar II disorder)

RESULTS

Patient Demographics

- Patient demographics showed a mean age of 35 ± 11 years; 71% female (Table 1)
- 31% of patients received ERC-CBZ monotherapy at initiation (Table 1); mean ERC-CBZ dose at best CGI-I was 581 ± 213 mg/d
- 68% of patients were diagnosed with bipolar I, 15% with bipolar II, and 17% with bipolar NOS (Table 1)
- 84% of patients were markedly ill at initiation of ERC-CBZ (CGI-S ≥5) (Figure 1)
- 51% of patients had comorbid conditions, with panic disorder, substance abuse, and anxiety disorder being the most frequent (Table 2)
- 69% of patients received at least 1 concomitant medication, with clonazepam (11%), escitalopram oxalate (10%), and venlafaxine (10%) being the most common



Characteristic	Percentage
Participants	300
Gender (% female)	71%
Mean age (SD)	35 (11)
Age range	18–75
ERC-CBZ monotherapy at initiation	31%
Bipolar subtype	
Bipolar I disorder	68%
Mixed	15.0%
Depressed	53.0%
Bipolar II disorder	15%
Bipolar NOS	17%

Condition	Percentage
At least 1 comorbid condition	51.0%
Comorbid Conditions Reported by 52% of ERC-CBZ-Treated Patients	
Panic disorder	16.7%
Substance abuse	14.3%
Generalized anxiety disorder	13.0%
Attention-deficit/hyperactivity disorder	9.7%
Alcohol abuse	8.0%
Post-traumatic stress disorder	4.0%
Obsessive-compulsive disorder	3.7%

Adverse Event	Percentage
Somnolence	11.0%
Dizziness	7.7%
Nausea	7.7%
Rash	5.0%
Headache	4.0%
Ataxia	3.7%
Increased appetite	3.7%

Characteristic	Manic/Mixed	Bipolar I	P Value
Participants	137	67	
Gender (% female)	71.9%	76.1%	.05†
Mean age (SD)	35.6 (10.7)	33.8 (11.3)	.22†
Clinical Global Impression–Severity (SD)	5.3 (0.8)	5.2 (0.9)	.90†
Clinical Global Impression–Improvement (SD)	2.4 (1.2)	2.5 (1.3)	.69†
Response	75.2%	71.6%	.71†
Relapse	35.0%	35.6%	.71†
Common Adverse Events			
Somnolence	8.9%	1.9%	.03†
Dizziness	2.2%	7.8%	.19†
Nausea	7.3%	7.9%	.91†
Rash	5.9%	7.6%	.33†

Characteristic	Manic/Mixed	Bipolar II	P Value
Participants	137	48	
Gender (% female)	71.9%	58.9%	.03†
Mean age (SD)	35.6 (10.7)	36.0 (10.2)	.79†
Clinical Global Impression–Severity (SD)	5.3 (0.8)	5.0 (0.7)	.12†
Clinical Global Impression–Improvement (SD)	2.4 (1.2)	2.5 (1.3)	.69†
Response	75.2%	68.9%	.02†
Relapse	35.0%	35.0%	.99†
Common Adverse Events			
Somnolence	8.9%	18.8%	.21†
Dizziness	2.2%	11.1%	.03†
Nausea	7.3%	13.3%	.16†
Rash	5.9%	2.2%	.27†

RESULTS (CONT)

Efficacy

- 73% of patients showed clinical response to ERC-CBZ treatment as assessed by CGI-I (Figure 2)
- 33% of responders demonstrated relapse (Figure 2)

Adverse Events

- Somnolence (11%), dizziness and nausea (8% each), and rash (5%) were the most prevalent adverse events (Table 3)

Comparisons by Bipolar Subtype

- Patients with bipolar I depression responded similarly to manic/mixed patients in treatment (72% vs 75%, respectively) (Table 4)
- Patients with bipolar II responded similarly to manic/mixed episode patients (69% vs 75%, respectively), except that dizziness was observed more frequently in the bipolar II population (11% bipolar II vs 2% manic/mixed; P = .03) (Table 5)

CONCLUSIONS

- In congruence with other ERC-CBZ studies,^{5,7} treatment was found to be effective (73% response) in this retrospective review of 300 adults with bipolar disorder
- Response to ERC-CBZ treatment was independent of subtype, as patients with bipolar I manic/mixed episodes responded similarly to patients with bipolar I depression and bipolar II disorder
- The incidence of adverse events was lower than those reported in previous acute 3-week studies,^{6,7} a result that may be attributable to a less aggressive outpatient titration schedule

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