

**DRUG DISPOSITION & PHARMACOKINETICS**

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## Switching from Other Agents to Extended-Release Carbamazepine in Acute Mania

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**ABSTRACT ~ Background:** There is a dearth of available knowledge relating to the efficacy of switching from one psychotropic agent to another in treating patients with acute mania. **Methods:** This is a post hoc analysis of data from two randomized, placebo-controlled trials of carbamazepine extended-release capsules (CBZ-ERC) in the treatment of mania, to evaluate the efficacy of CBZ-ERC in patients previously nonresponsive to lithium ( $n = 40$ ), olanzapine ( $n = 38$ ), or valproate (VPA,  $n = 77$ ). **Results:** In patients previously on lithium, Young Mania Rating Scale (YMRS) scores improved significantly from baseline to end point ( $27.4 \pm SD 3.5$  vs.  $15.8 \pm 11.1$ ;  $P = .0002$ ). In patients previously on VPA or olanzapine, YMRS scores significantly improved in both CBZ-ERC- and placebo-treated groups (VPA: CBZ-ERC,  $P < .0001$ ; placebo,  $P = .0002$ ; olanzapine: CBZ-ERC,  $P < .0001$ ; placebo,  $P = .0054$ ). Improvement in YMRS was significantly greater in CBZ-ERC-treated patients versus placebo in subjects previously nonresponsive to lithium (CBZ-ERC  $11.6 \pm 10.3$  vs. placebo  $4.0 \pm 11.2$ ,  $P = .03$ ), or VPA (CBZ-ERC  $10.8 \pm 11.9$  vs. placebo  $5.7 \pm 9.2$ ;  $P = .04$ ), and trending to be greater for those previously nonresponsive to olanzapine (olanzapine  $13.2 \pm 9.3$  vs. placebo  $7.3 \pm 9.7$ ,  $P = .06$ ). **Conclusions:** CBZ-ERC is an effective therapy for bipolar patients previously nonresponsive to lithium or valproate. Medication switch is

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*frequently associated with symptom improvement.* Psychopharmacology  
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## INTRODUCTION

Although a multitude of agents have been shown to be effective in the treatment of acute mania, the illness remains difficult to treat. Rates of nonresponse range from one third to one half of acutely ill manic patients<sup>1,2</sup> and polypharmacy is commonly required.<sup>3</sup> Additionally, non-adherence and partial adherence are common in bipolar illness,<sup>4,5</sup> frequently because of the adverse effects<sup>6,7</sup> and poor insight,<sup>8,9</sup> giving the impression of nonresponse. For these reasons, the need for switch of pharmacologic agent arises frequently in bipolar treatment (36.6%<sup>10</sup>). However, there is a dearth of data regarding the efficacy of switching agents, and most of the available studies examine switching neuroleptic agents in schizophrenia.<sup>1,11</sup>

This study analysis was undertaken to glean insights into the results of switching agents in acutely ill manic or mixed patients. Patients who were previously on lithium, valproate, or olanzapine, and who were still significantly symptomatic were switched to extended-release carbamazepine capsules (CBZ-ERC) or placebo and followed for 3 weeks. Primary response was measured with the Young Mania Rating Scale (YMRS). Secondary outcome measures included clinicians' global impression and the Hamilton Depression Rating Scale (HDRS).

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