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## **Tamoxifen: An Intracellular Target for Treatment of Mania**

*Another small, positive study for a drug that alters intracellular dynamics*

Investigators have begun to elucidate complex changes in intracellular dynamics in mood disorders. The ubiquitous intracellular enzyme protein kinase C (PKC) seems to show increased activity in bipolar disorder. To evaluate the efficacy of tamoxifen, an estrogen receptor antagonist that inhibits PKC ([Journal Watch Psychiatry Nov 5 2007](#)), investigators in Turkey randomized 66 inpatients with mania to receive tamoxifen or placebo for 3 weeks.

The hospital provided structured activities, allowed adjunctive lorazepam, and permitted relatives to stay with patients. Few patients (tamoxifen recipients, 17%; placebo recipients, 32%) dropped out. Scores on a standardized mania scale increased in placebo recipients but decreased in tamoxifen recipients. Scores at 3 weeks were significantly different, as were response rates (50% reduction in mania scores; tamoxifen, 44%; placebo, 4%; number needed to treat, 2.51). Lorazepam was used significantly less frequently with tamoxifen than with placebo.

**Comment:** Compared with patients in industry-sponsored studies on antimanic properties of atypical antipsychotics and some anticonvulsants, the patients here were considerably more ill, and some were treatment-refractory. These factors may account for the lower placebo response rate, the smaller number of dropouts, and the somewhat lower response rate in this study than in brief industry-sponsored studies that led to the adoption of atypical antipsychotics and anticonvulsants as antimanic drugs. As is true of most patients receiving monotherapy for mania, few of these mania patients were well at the end of this brief course of treatment.

Researchers hypothesize that bipolar disorder elevates intracellular calcium-ion signaling and increases activation of a G-protein linked to the membrane enzyme system that activates PKC in association with intracellular calcium mobilization. The calcium channel blockers verapamil and nimodipine have shown similar efficacy for bipolar disorder in small studies. Further investigations of intracellular targets may lead to more predictable and effective therapies for bipolar disorder.

— [Steven Dubovsky, MD](#)

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