

Calming The Roller-Coaster Ride, Bipolar Disease: A Double-Blind, Active Controlled Trial Demonstrates Anti-Manic Efficacy Of A New Protein Kinase C Inhibitor Endoxifen

Ateeq Ahmad Ph.D.
Jina Pharmaceuticals Inc.,
USA





Outline

✓ Drugs for **Bipolar Disorder I** Protein Kinase C Inhibitors

✓ Clinical Trial Design
Safety & Efficacy



✓ Efficacy  (YMRS)

✓ PK-PD (Exposure-Response)



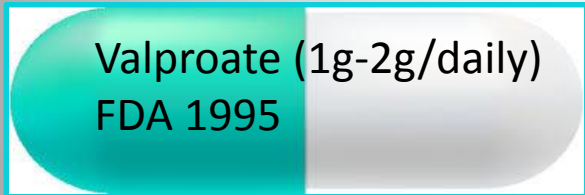
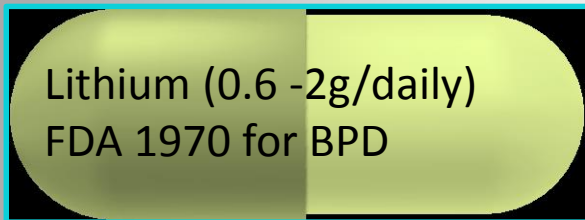
✓ Onset of Action Compared with Known Drugs



✓ Summary

Drugs for Bipolar Disorder I

Common Drugs



FDA 2000

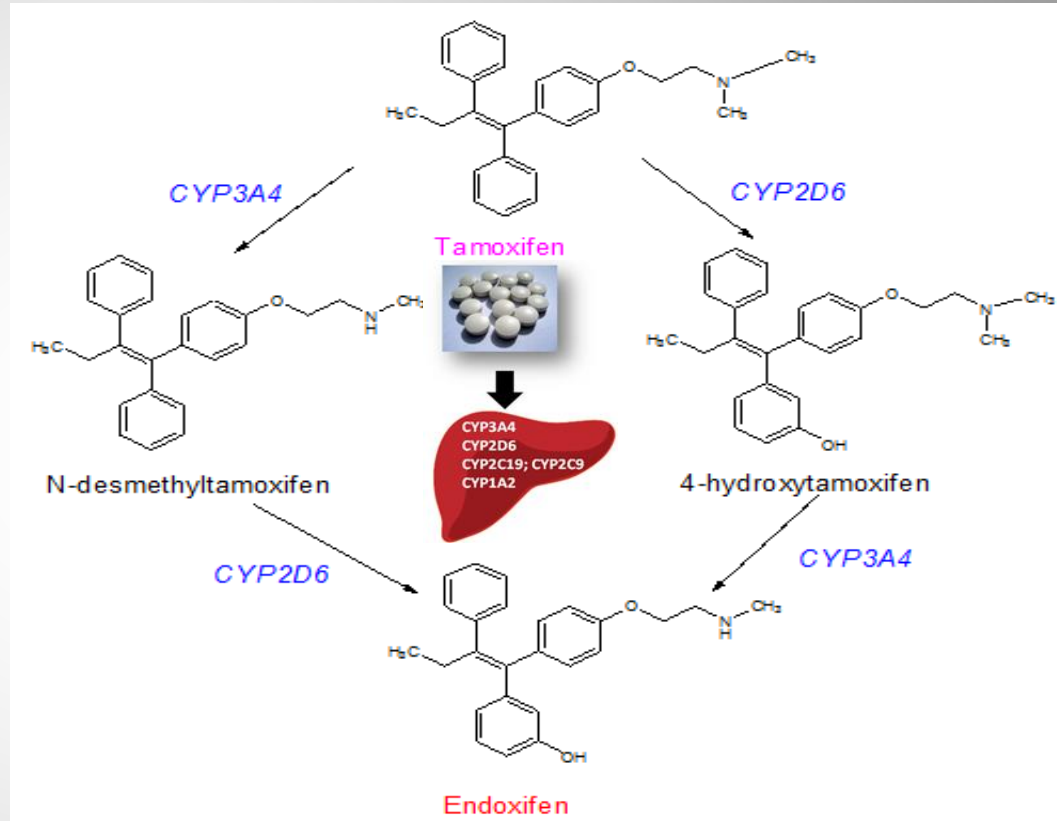
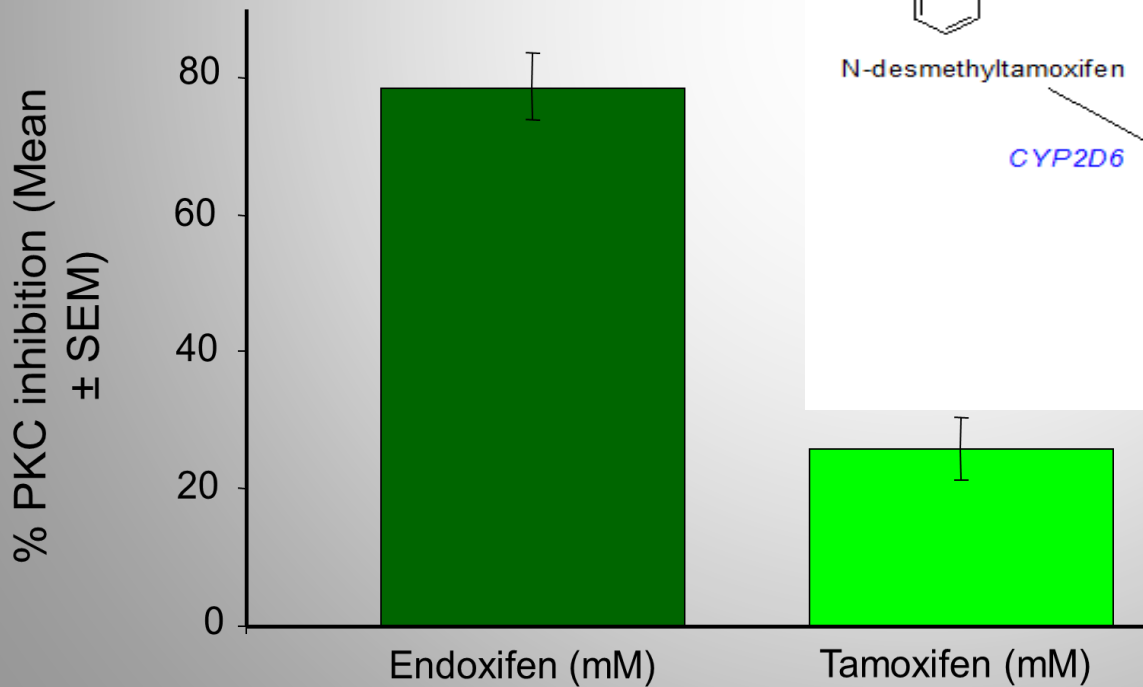


Issues and Side Effects

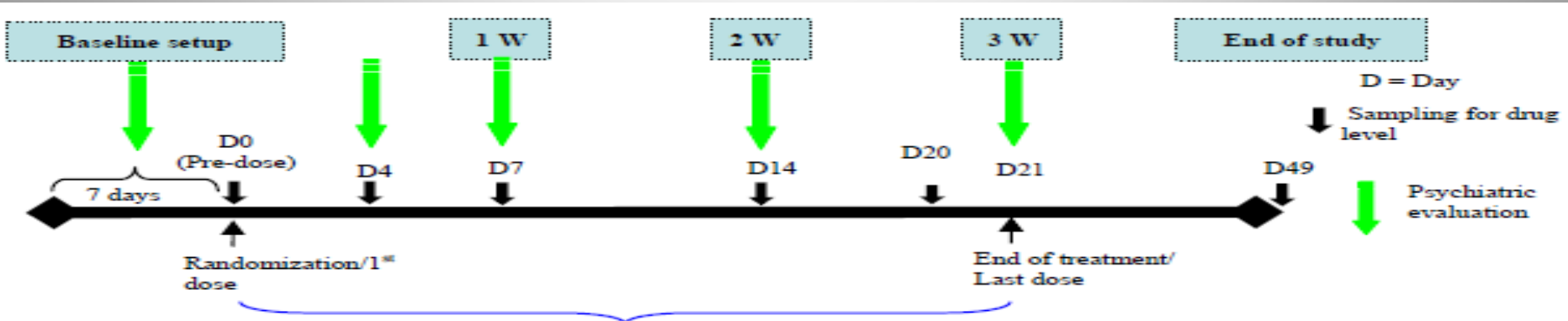
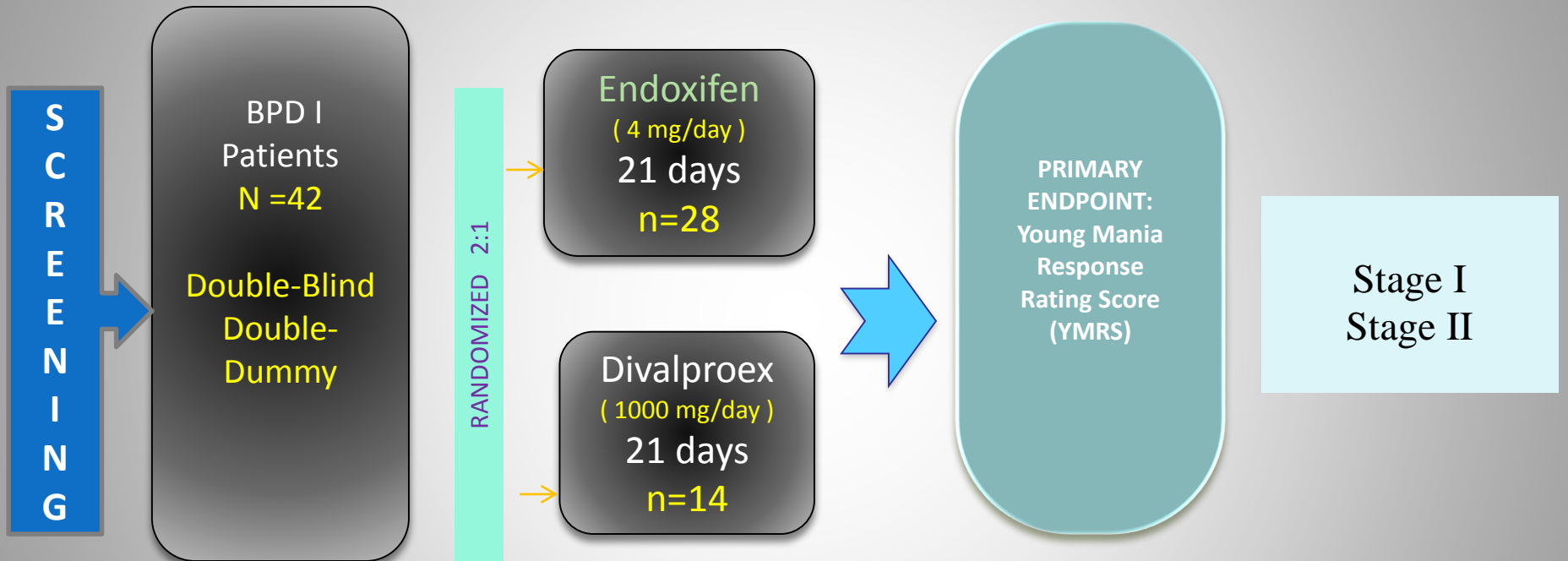
- ✓ **Weight Gain**
- ✓ **Extra Pyramidal Symptoms**
 - ✓ Akathisia: "Inability to sit"
 - ✓ Pseudoparkinsonism

Narrow Therapeutic Index

Protein Kinase C Inhibitors for BPD



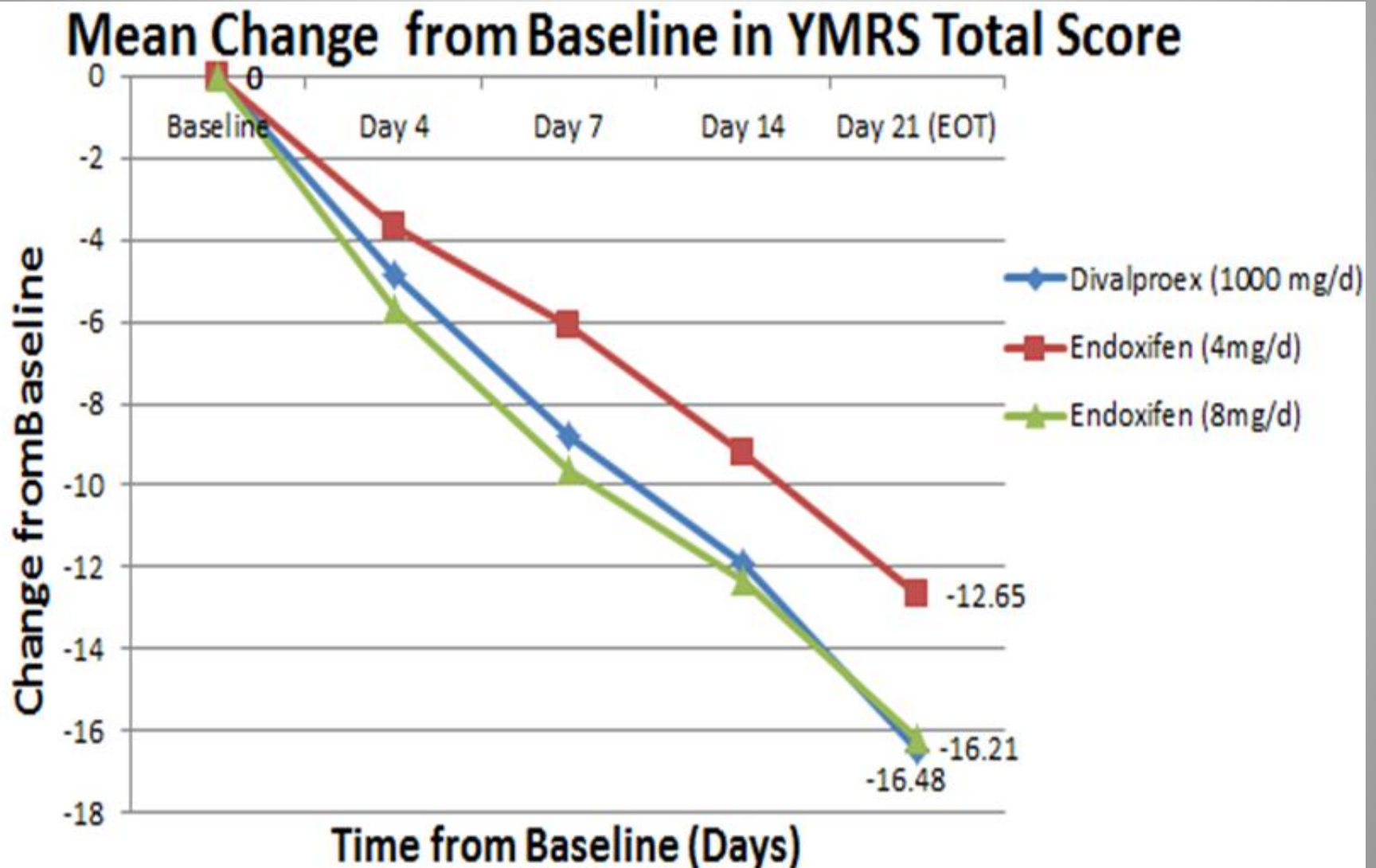
Endoxifen - Clinical Trial Design



Endoxifen -Safety & Efficacy

	E (4mg/d) N=27	E (8 mg/d) N=28	D (1 gm/d) N=28
	n (%)	n (%)	n (%)
Safety			
Patients with at least one AE	8 (29.63)	7 (25)	12 (41.38)
Nausea	1 (3.7)	1 (3.57)	5 (17.24)
Insomnia	1 (3.7)	2 (7.4)	5 (17.24)
Efficacy			
Proportion of Responders	12 (44.44)	18 (64.29)	21(72.41)

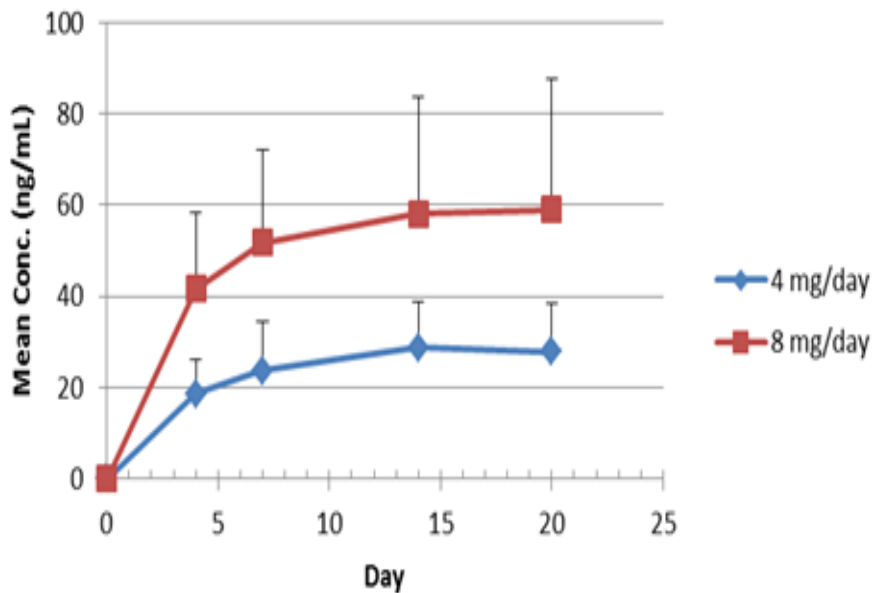
Improvement in YMRS score for Endoxifen



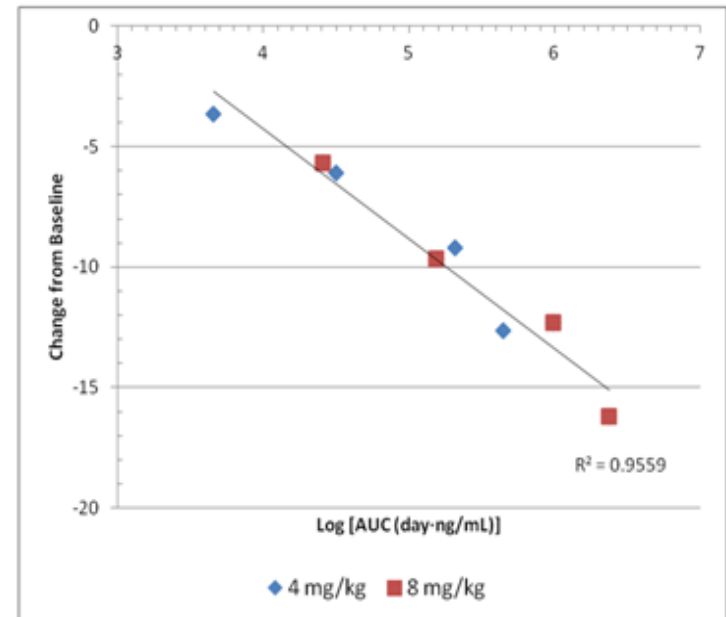
Exposure-Response Analysis of Endoxifen

Exposure-Response Analysis of Endoxifen

Plasma Conc. - Time Profile of Endoxifen



Endoxifen AUC - Changes in Total YMRS Score from Baseline



Endoxifen - Rapid Onset of Action

Monotherapy Trials of drugs for the treatment of Bipolar Disorder I Trial Duration (3 weeks)

Treatment	Baseline YMRS Score	Change from Baseline	Onset of Action (days)
Divalproex (1 g/day)	28	-4.86	4
Endoxifen (mg/day) 4	24	-3.65	4
8	27	-5.66	4

Summary

- Endoxifen
 - Safe
 - Potent PKC inhibitor
 - Efficacy demonstrated by change in YMRS Score
 - **Exposure**-Response (PK-PD) Analysis shows proportionality
 - Rapid Onset of action in BPD patients

ateeq@jinapharma.com

(847) 573 0731

