

Workshop: Clinical Trials

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Disclosure / conflicts of interest

Concept

Company

Research

AB-Biotics, Abbvie, Almirall, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Celon, Cephalon, Dainippon Sumitomo Pharma, Elan, Ferrer, GH Research, GlaxoSmithKline, Janssen, Lilly, Lundbeck, Orion, Otsuka, Pfizer, Sanofi-aventis, Servier, Sunovion, Takeda

Education

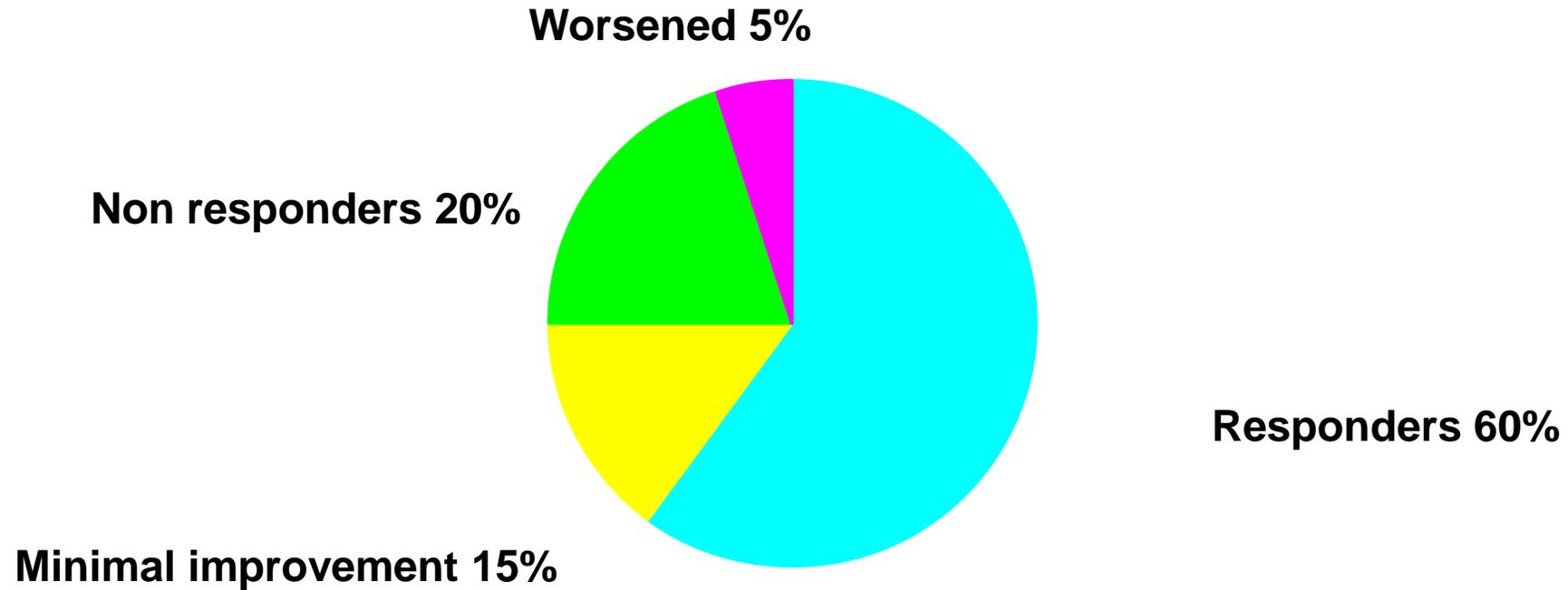
Abbott, Abbvie, Angelini, AstraZeneca, Bristol-Myers Squibb, Cambridge University Press, Elsevier, Farmindustria, Ferrer, Galenica, GlaxoSmithKline, Janssen, Johnson & Johnson, Lilly, Lundbeck, Oxford University Press, Otsuka, Pfizer, Sanofi-aventis, Viatrix

Consultancy

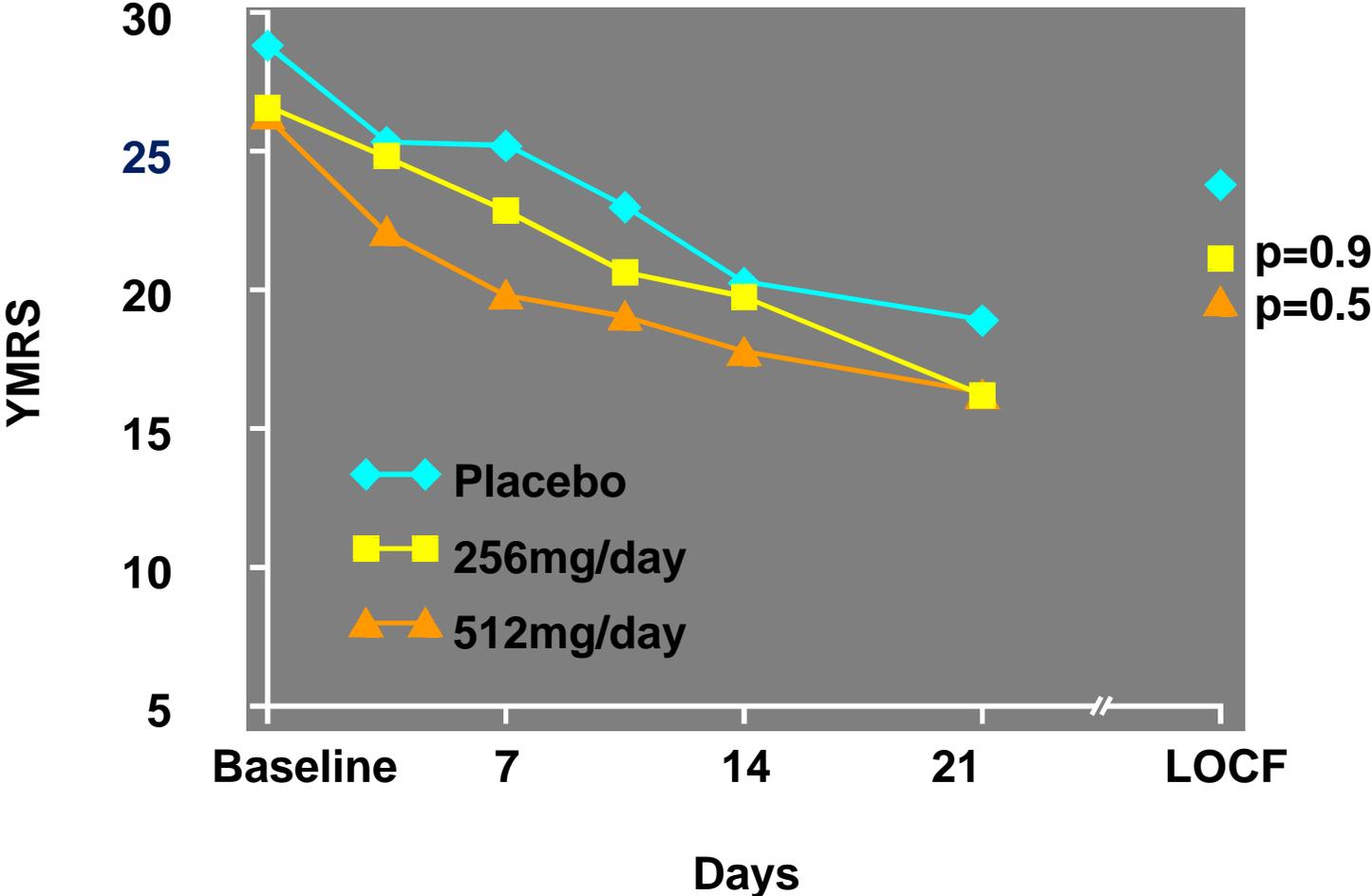
Abbvie, Angelini, AstraZeneca, Biogen, Biohaven, Bristol-Myers Squibb, Celon, Compass, Ferrer, GH Research, Gedeon Richter, HMNC, Idorsia, Janssen, Jazz, Lilly, Lundbeck, Merck Sharp & Dohme, Novartis, Organon, Otsuka, Pfizer, Roche, Sage, Sanofi-aventis, Servier, Shire, Sunovion, Takeda, Teva



Topiramate vs. placebo in Mania (open study)

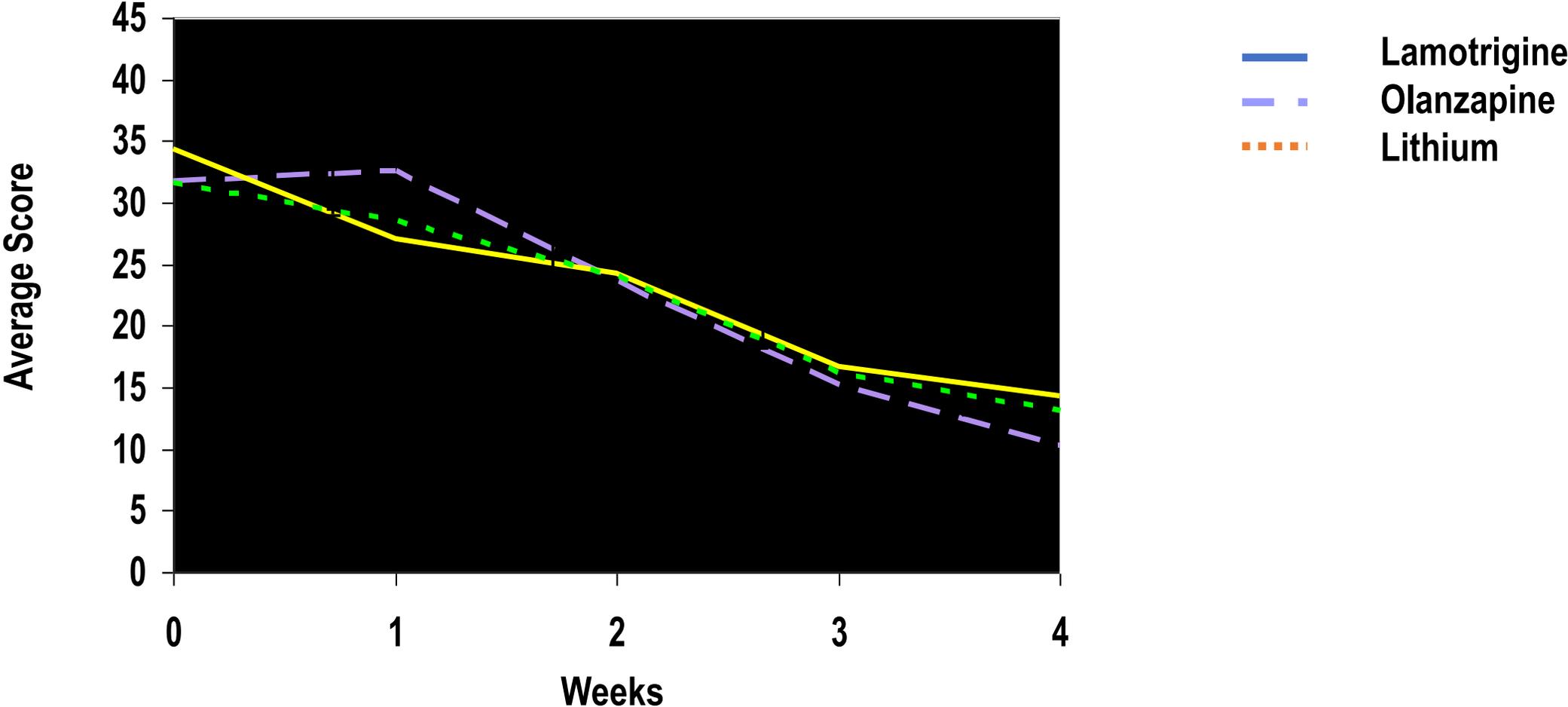


Topiramate vs. placebo in Mania (final sample; n=97)



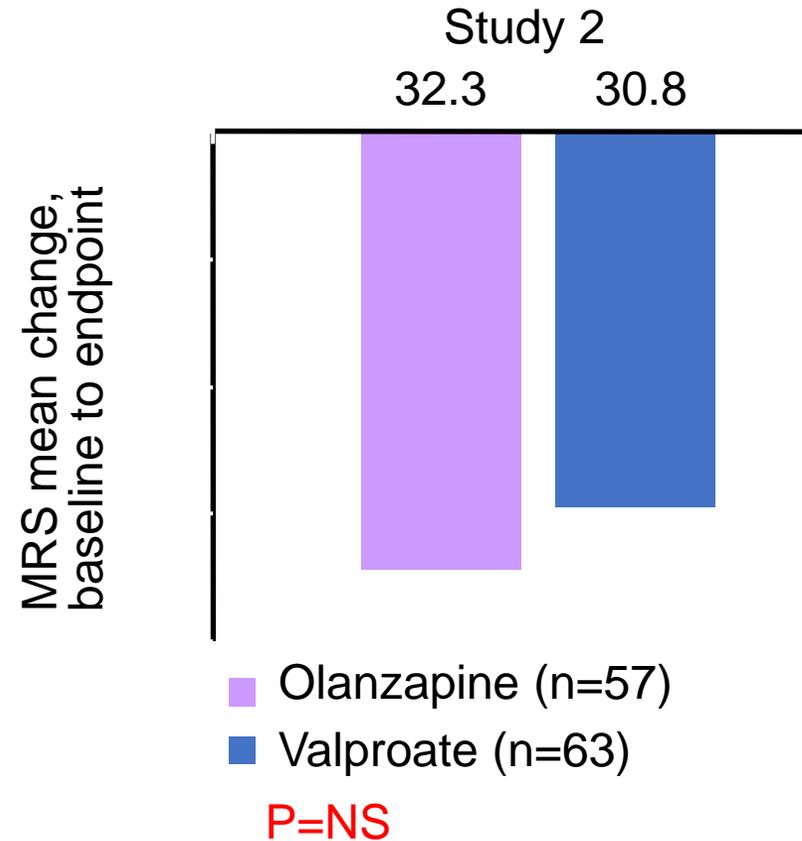
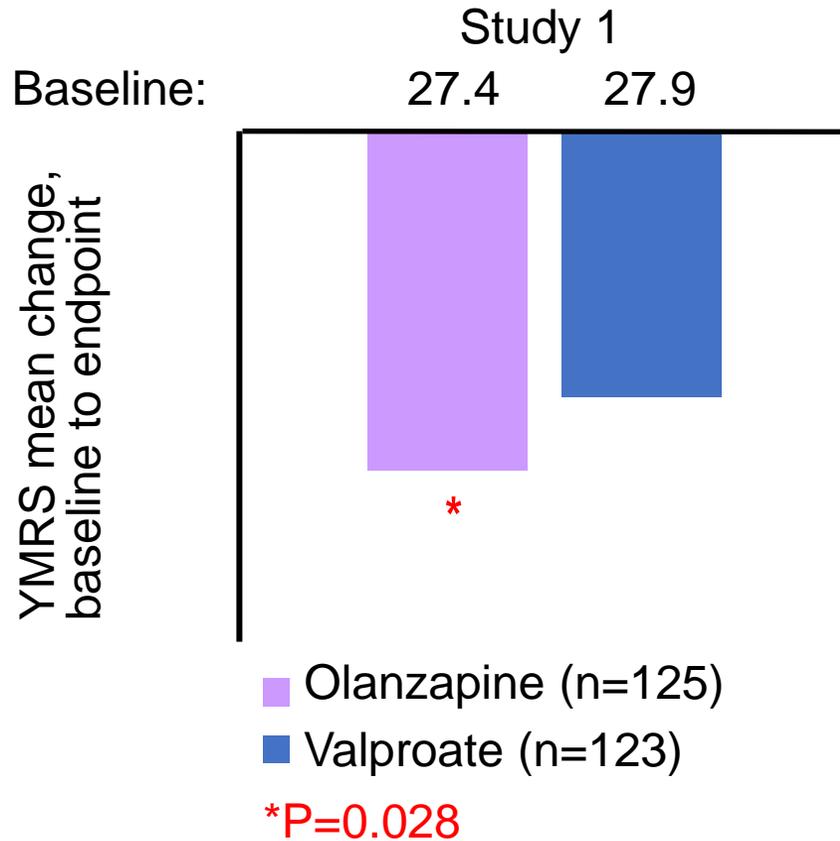
Chengappa et al, *Bipol Disord* 2001.

Olanzapine, Lamotrigine and Lithium in Mania



Berk M et al. *Int Clin Psychopharmacol.* 1999;14(6):339-343.

Possible Superiority of Olanzapine vs. Valproate in Mania



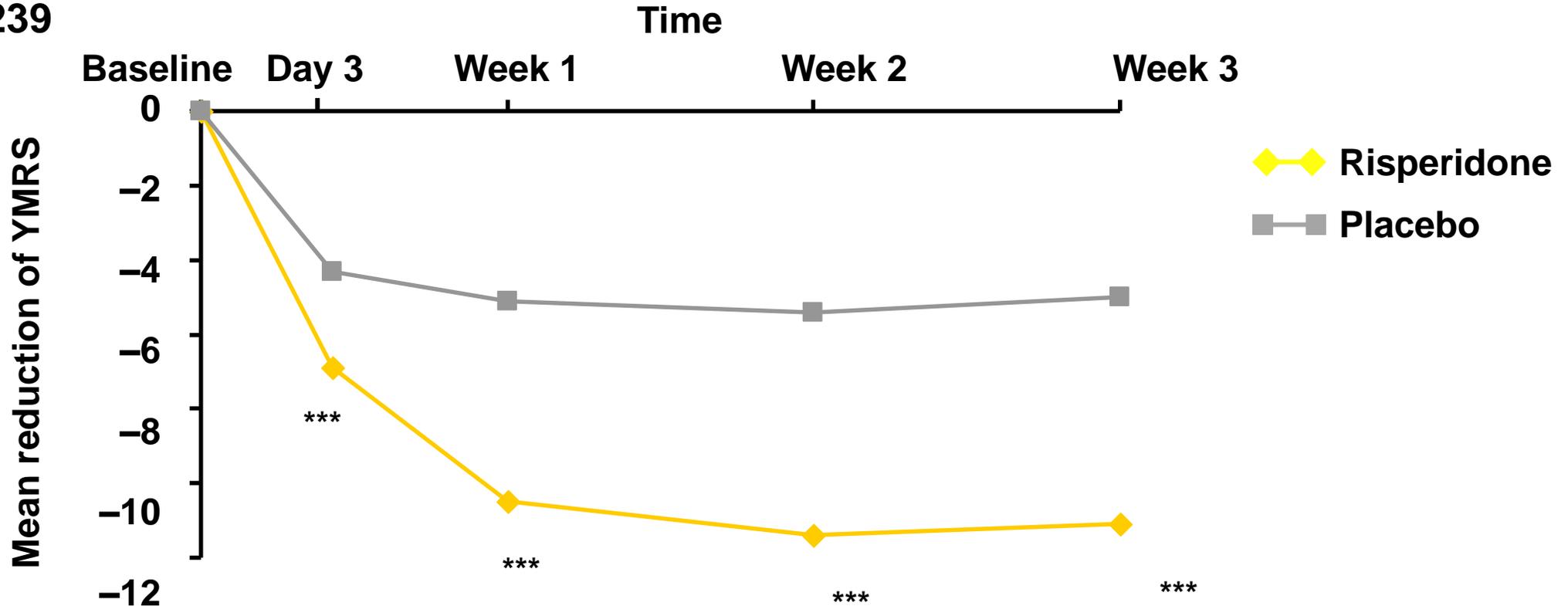
Tohen et al. *Am J Psychiatry* 2002; 159:1011–1017

Zajacka et al. *J Clin Psychiatry* 2002; 63:1148–1155

Vieta. *J Clin Psychiatry* 2003; 64: 1266-1267.

Antimanic efficacy of risperidone monotherapy

RIS-USA-239

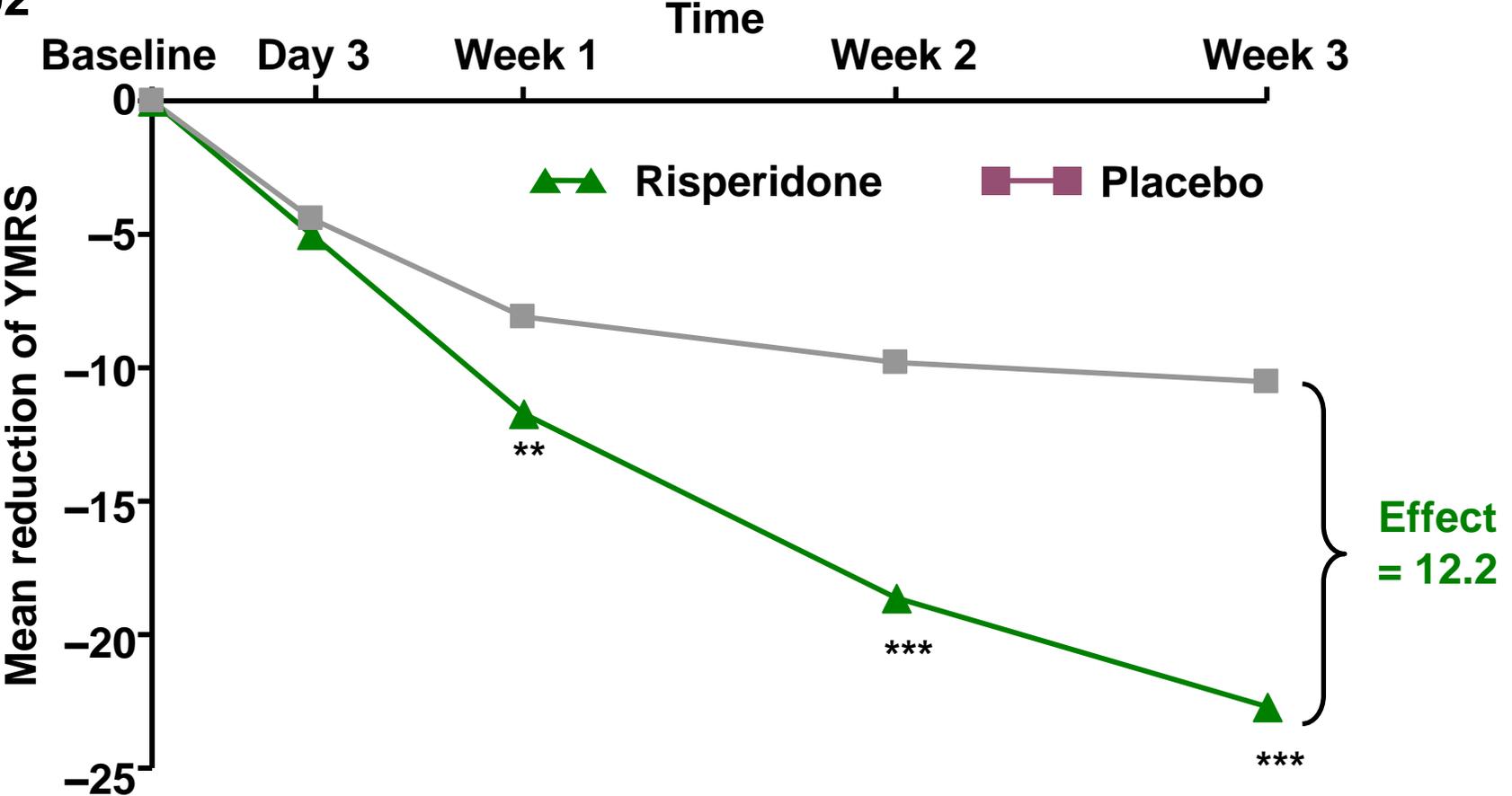


LOCF analysis; ***p<0.001 risperidone vs placebo
Baseline YMRS = 29; Final YMRS= 18
LOCF = last observation carried forward

Hirschfeld et al. Am J Psychiatry, 2004.

Antimanic efficacy of risperidone monotherapy

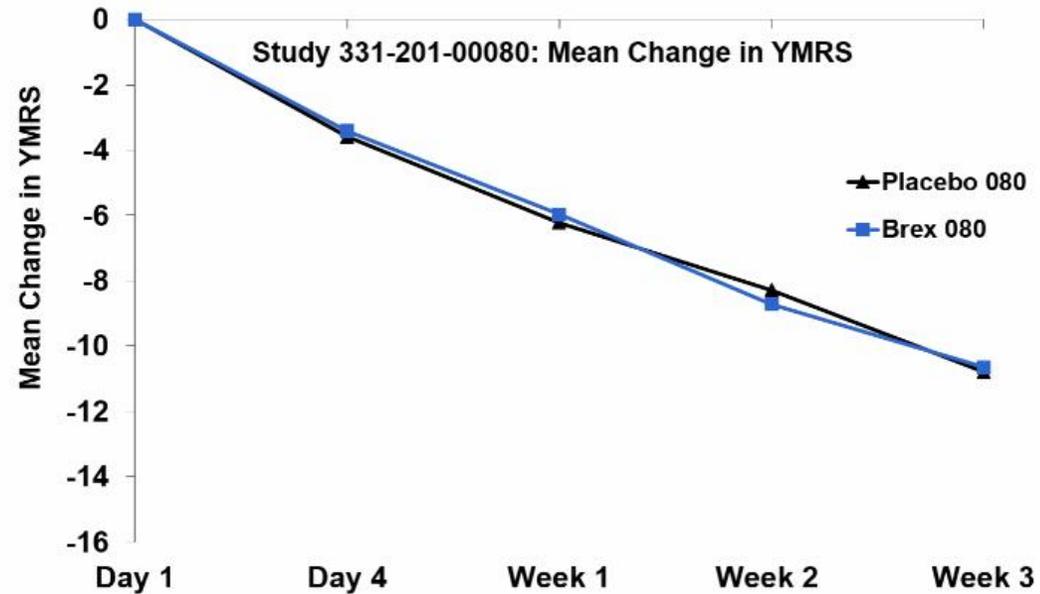
RIS-IND-002



LOCF analysis; **p<0.01; ***p<0.001 vs placebo
Baseline YMRS = 37;
Final YMRS = 15

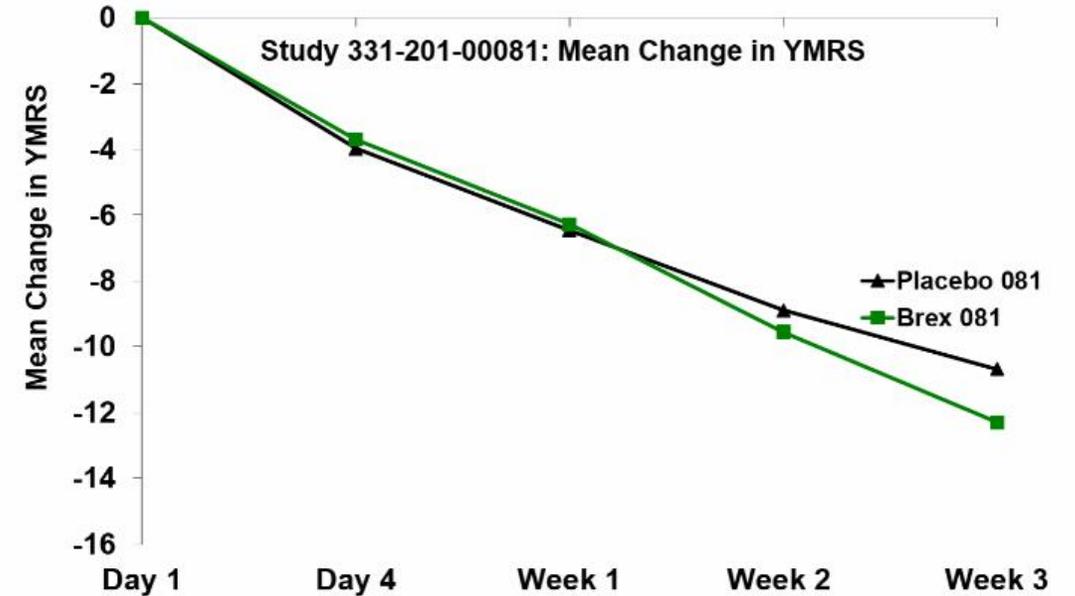
Brexpiprazole in Mania

331-201-00080 Primary Endpoint: YMRS Total Score
(MMRM UN; Efficacy Sample)



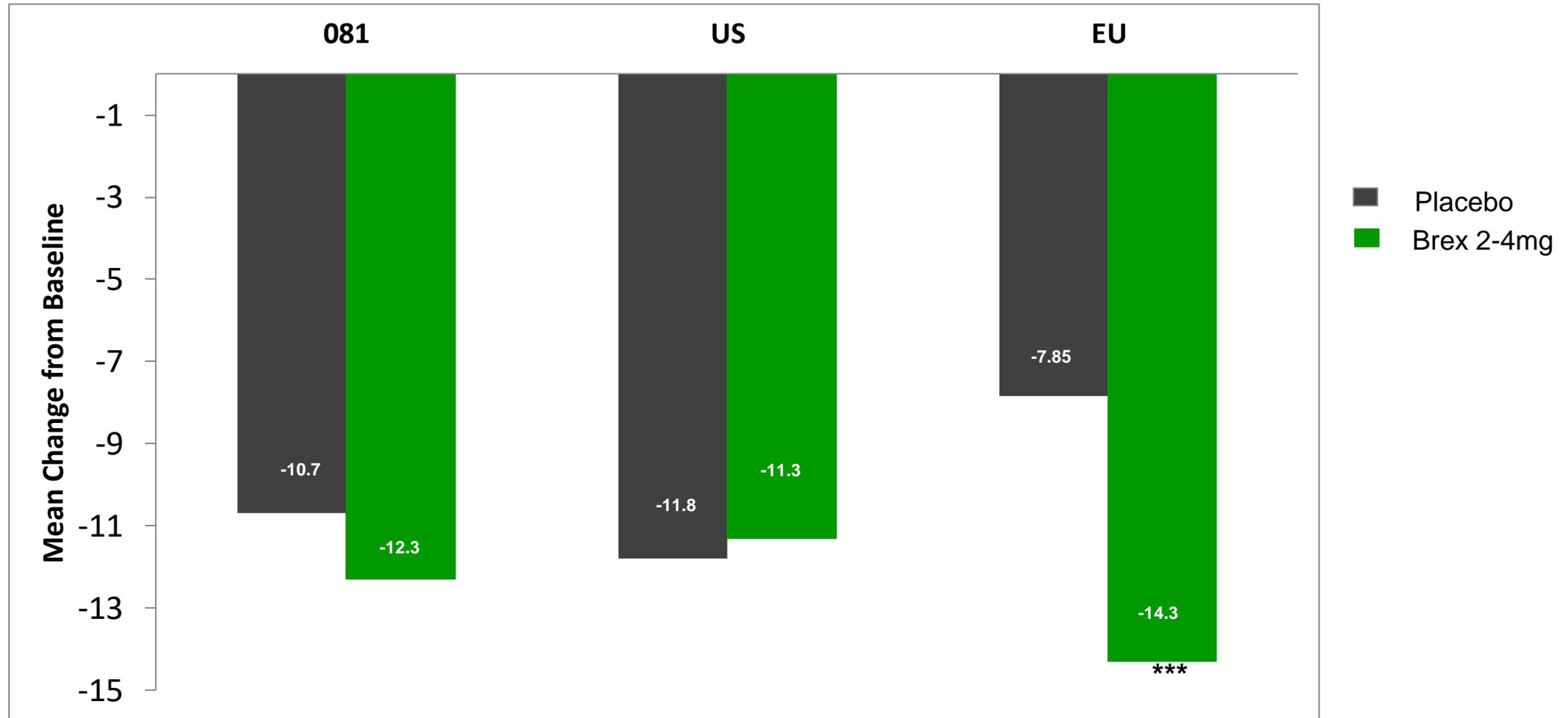
Brexpiprazole 080: Baseline YMRS Placebo = 30.55, n = 161, Brexpiprazole 2-4 mg = 30.39, n = 158

331-201-00081 Primary Endpoint: YMRS Total Score
(MMRM UN; Efficacy Sample)



Brexpiprazole 081: Baseline YMRS Placebo = 30.71, n = 168, Brexpiprazole 2-4 mg = 30.75, n = 162

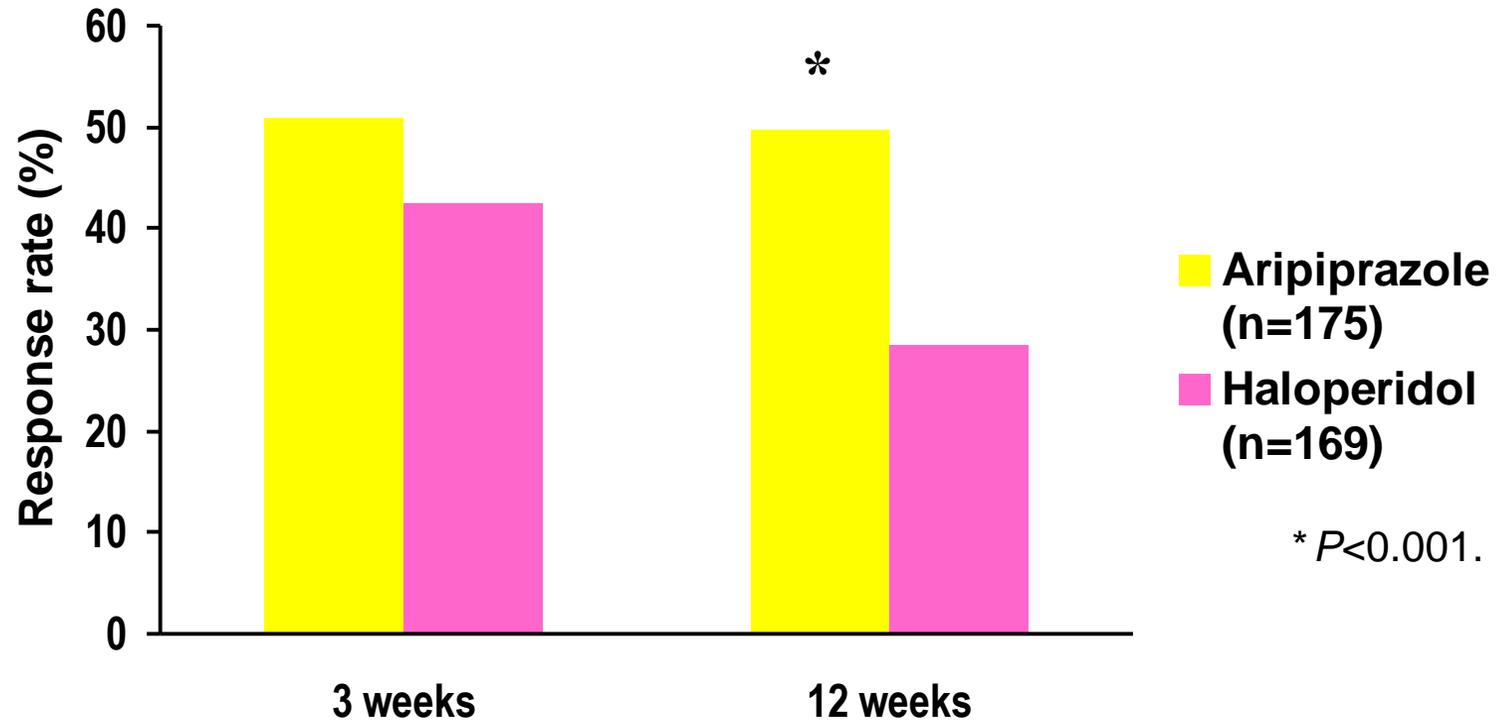
Brexpiprazole mania trial: regions



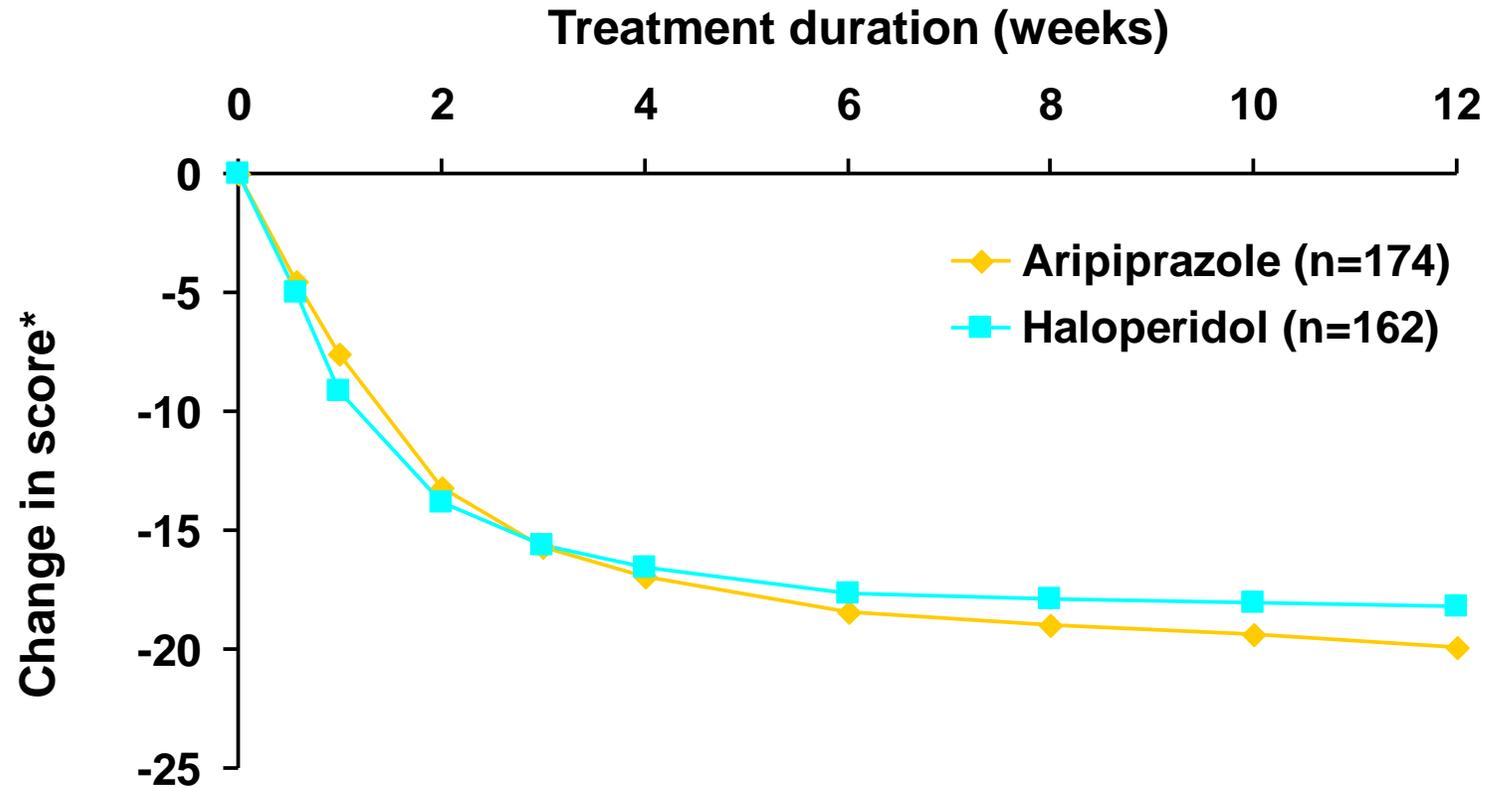
+p<0.10, * p < 0.05, ** p < 0.01, *** p < 0.001

Brexpiprazole 081: Baseline YMRS Placebo = 30.71, n= 168 Brexpiprazole 2-4 mg = 30.75, n = 162
Brexpiprazole 081 US: Baseline YMRS Placebo = 30.44, n = 120, Brexpiprazole 2-4 mg = 30.56, n = 117
Brexpiprazole 081 EU: Baseline YMRS Placebo = 31.38, n = 48, Brexpiprazole 2-4 mg = 31.24, n = 45

Aripiprazol vs Haloperidol in Mania



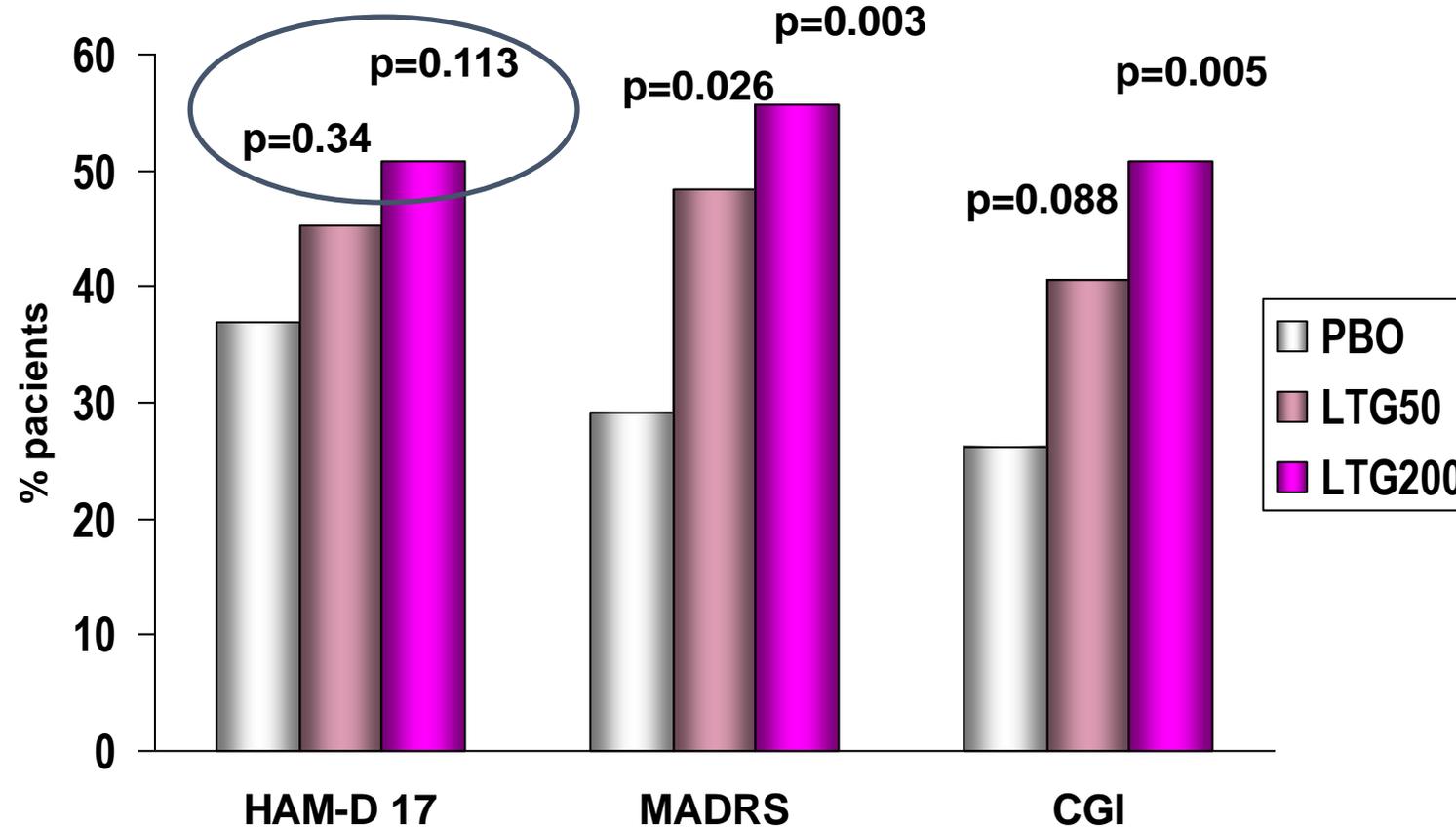
Aripiprazol vs Haloperidol in Mania



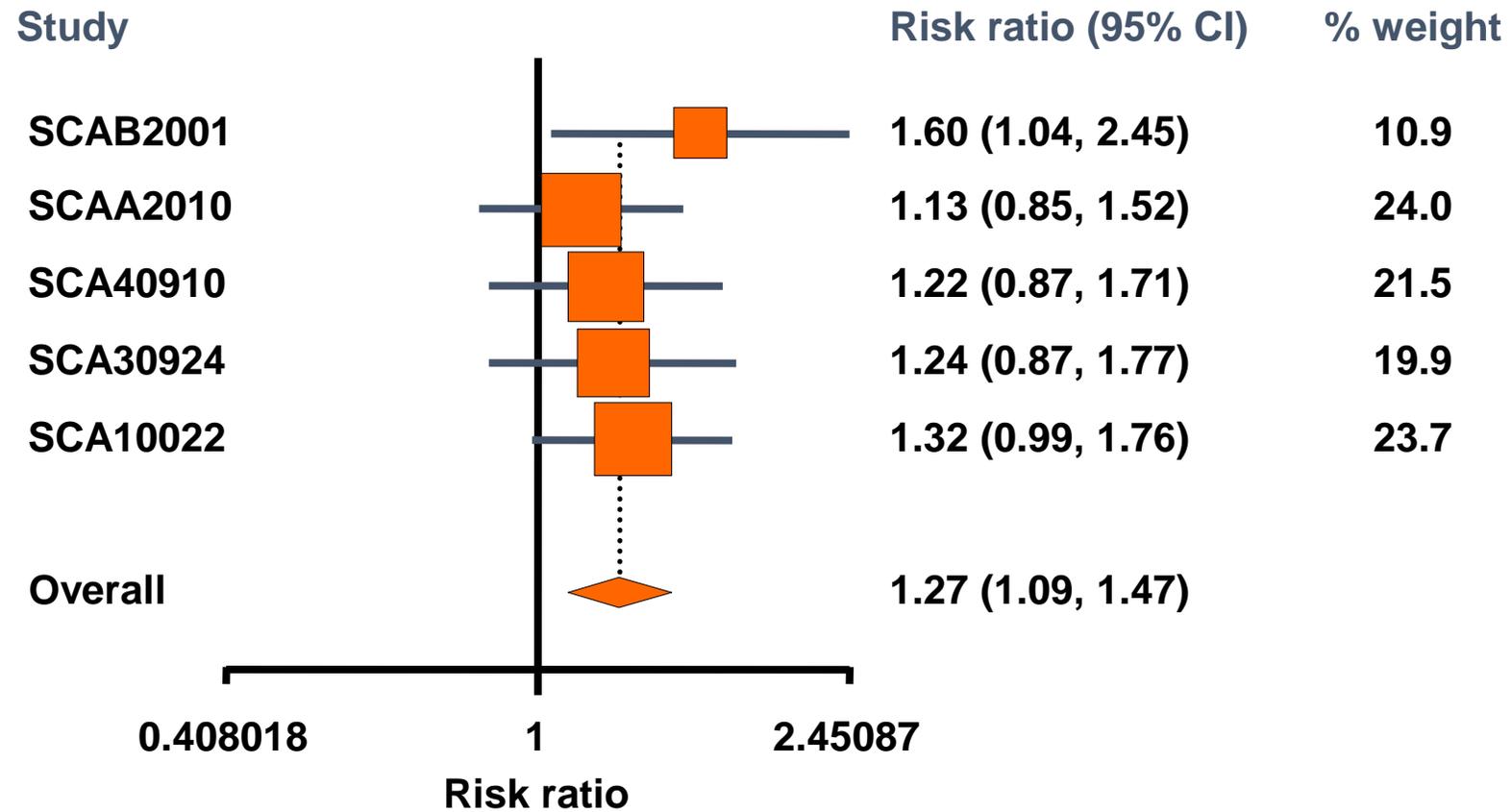
*Baseline Y-MRS scores: aripiprazole = 31.07, haloperidol = 31.39

Lamotrigine Response in Bipolar Depression

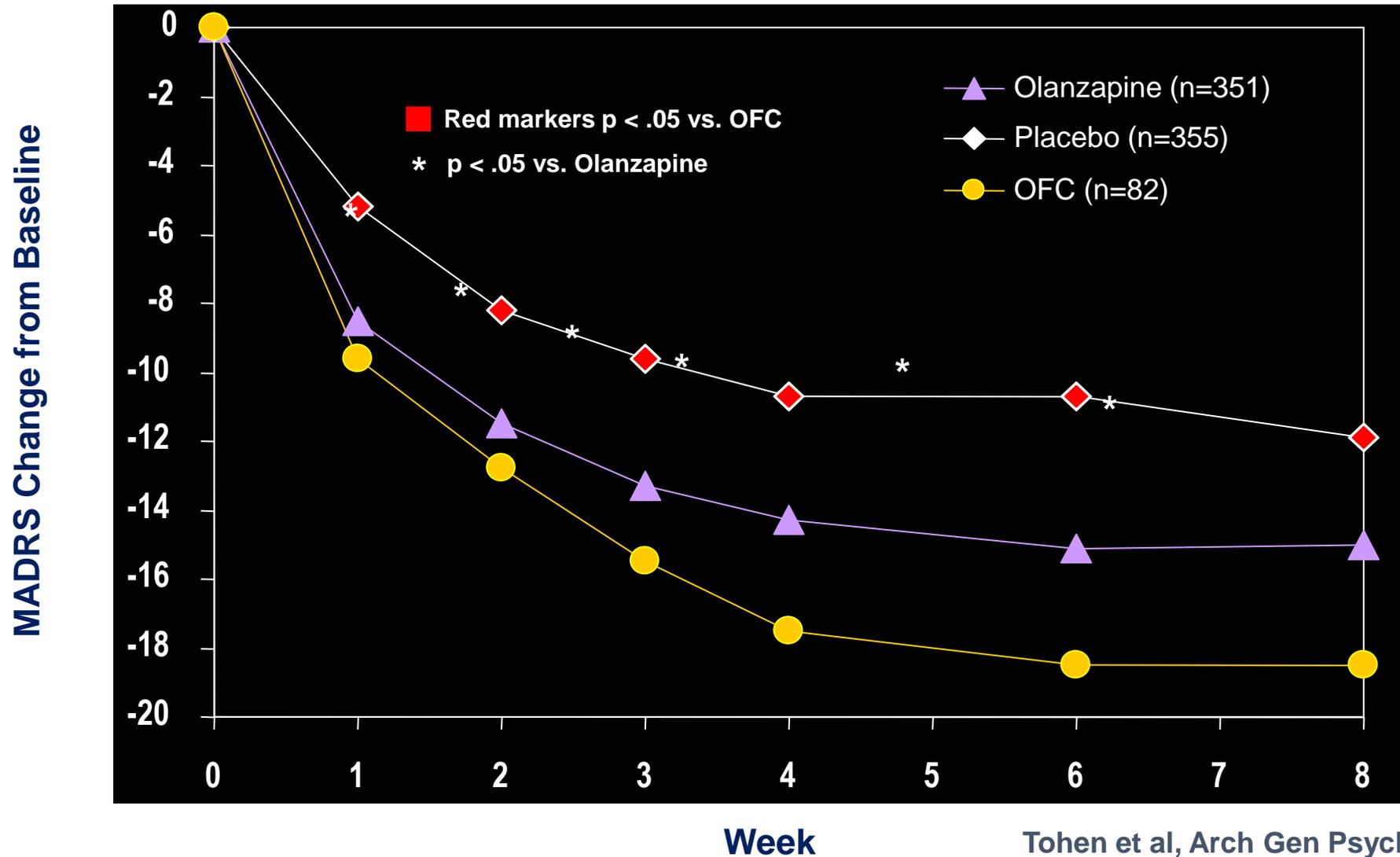
(Decrease \geq 50% in front of baseline or CGI-I of 1-2)



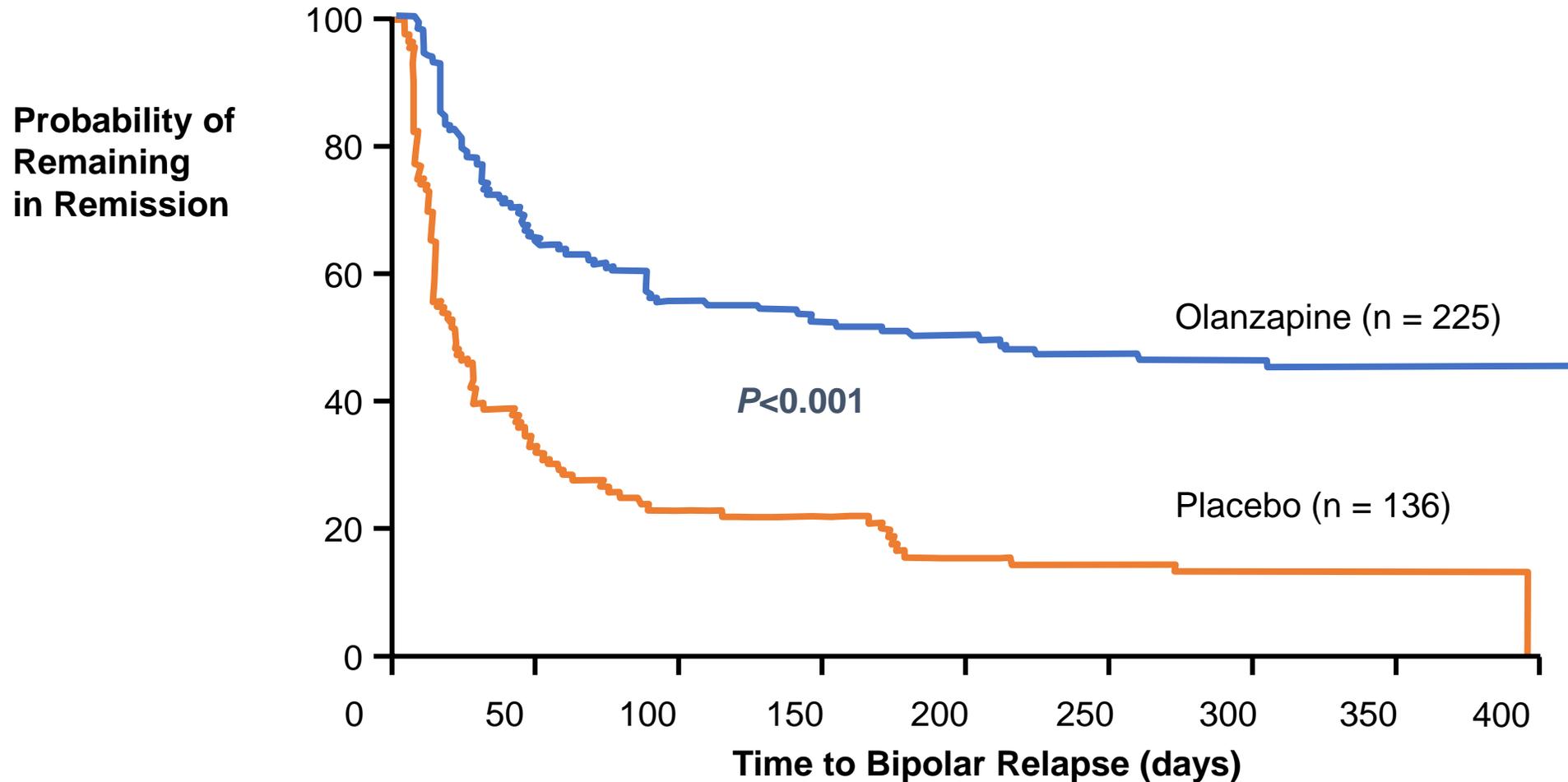
Meta-analysis of Lamotrigine in bipolar depression



Olanzapine in Bipolar Depression

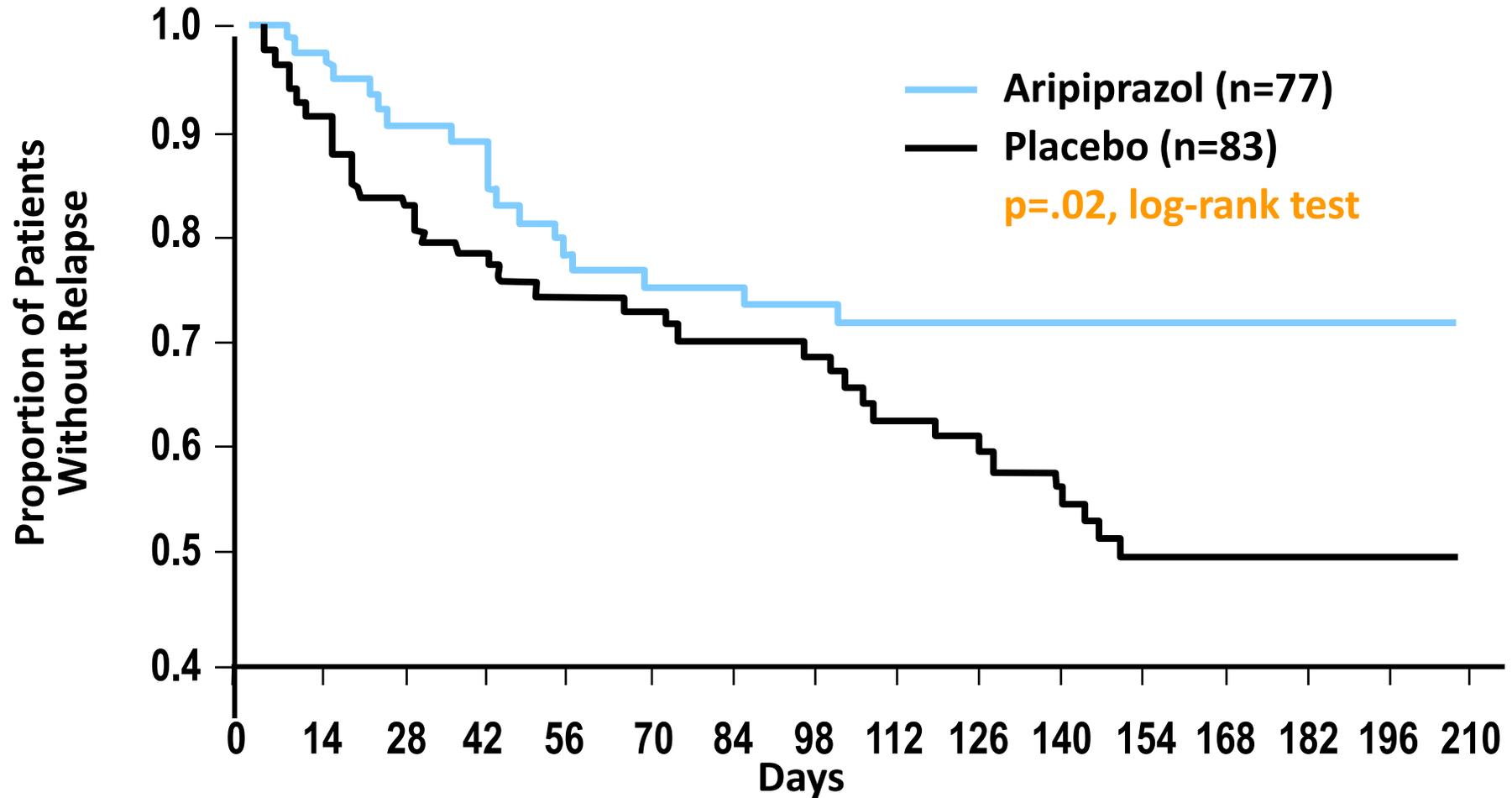


Olanzapine vs Placebo: Time to Recurrence of Mood Episode

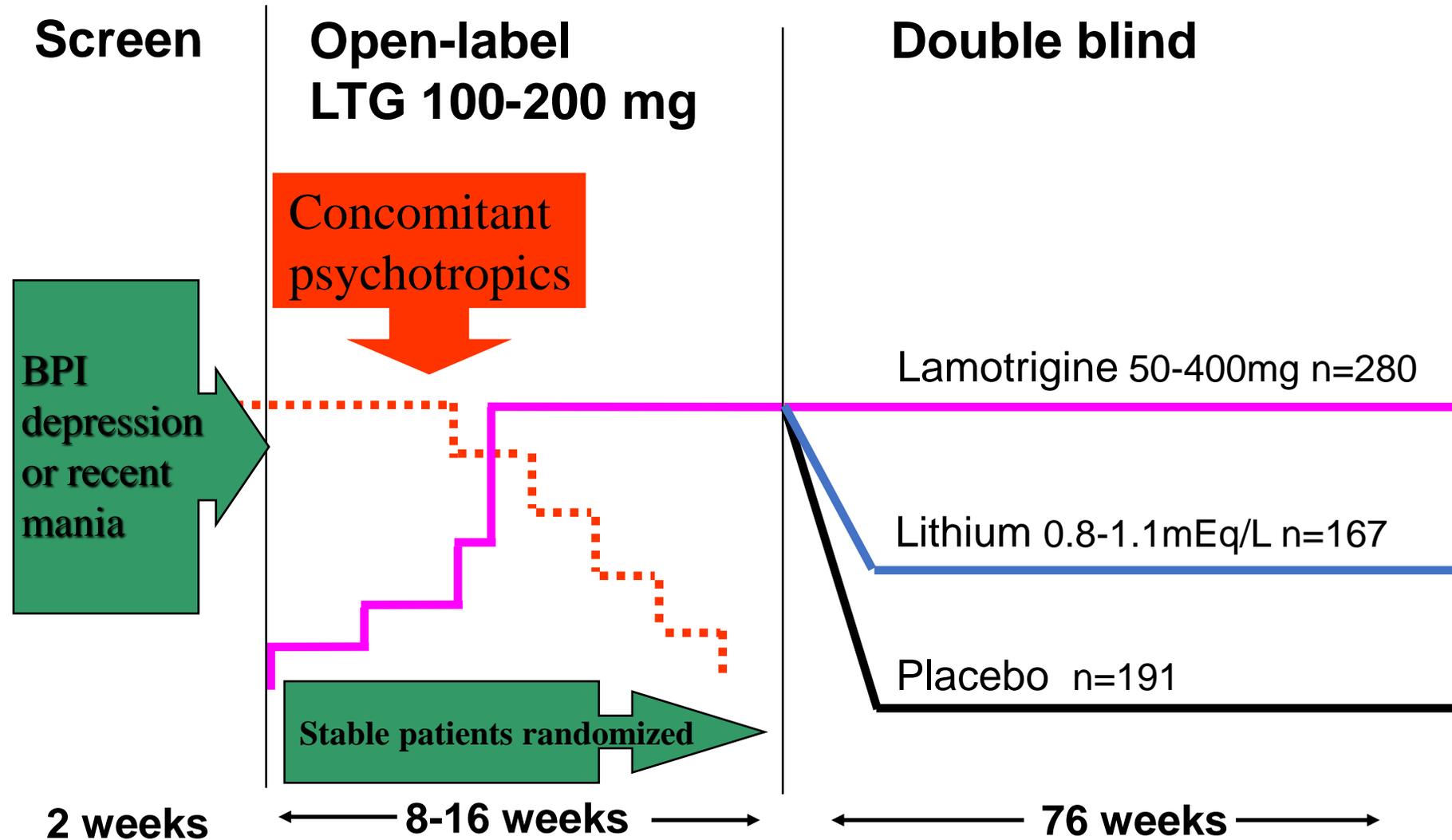


Recurrence = YMRS and/or HAMD-21 total scores ≥ 15 .
Tohen M et al. *Am J Psychiatry*. 2006;163(2):247-256.

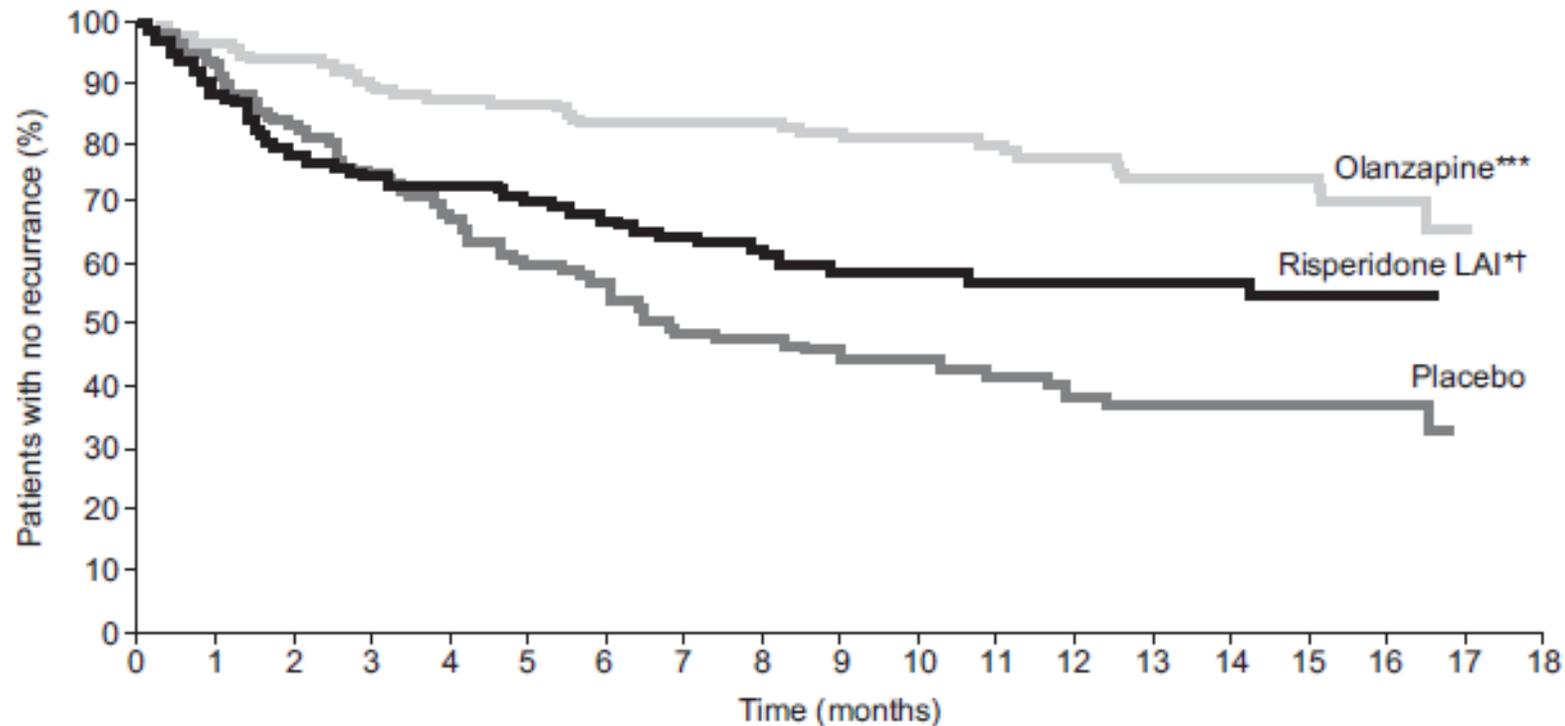
Aripiprazole vs Placebo: Time to Recurrence of Mood Episode



Lamotrigine: Clinical Trials 605/606



Long acting injectable risperidone versus oral olanzapine versus placebo



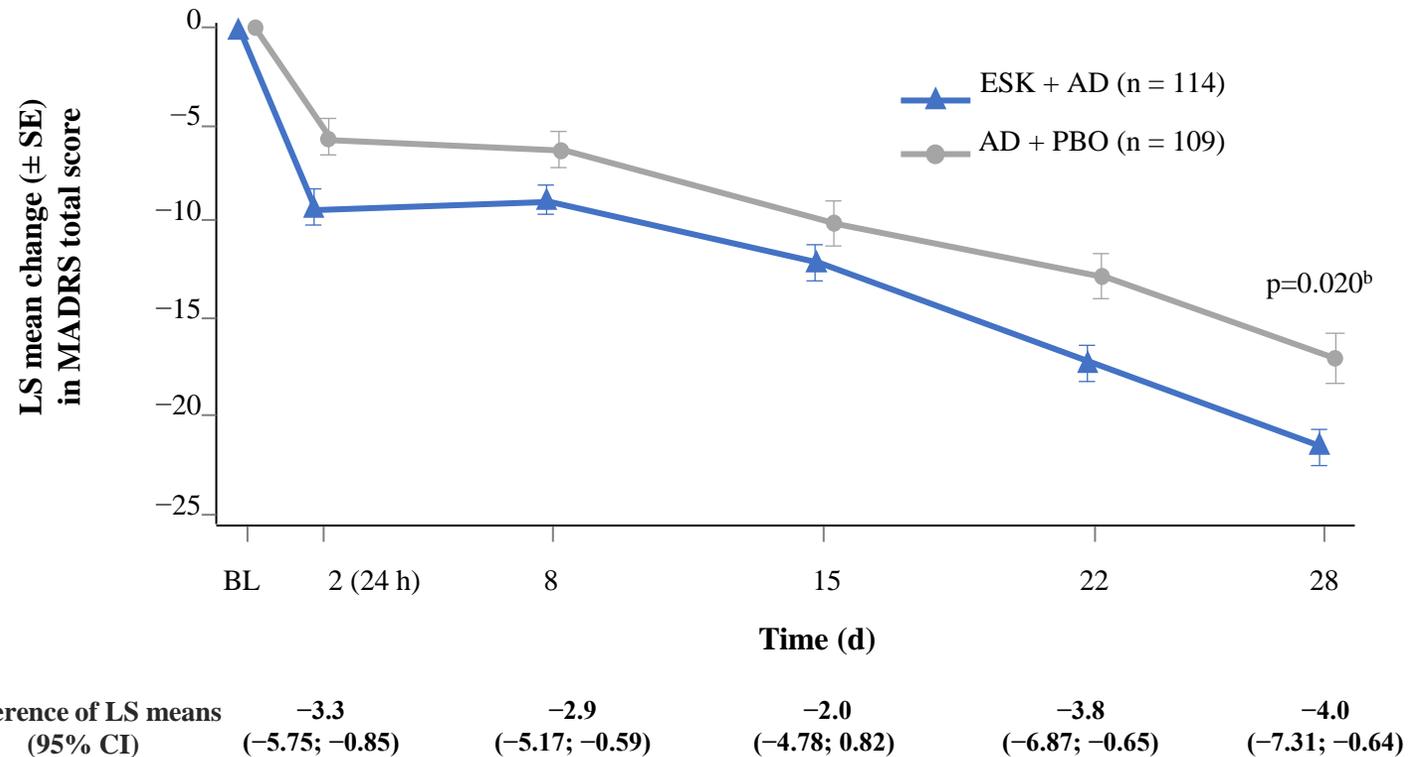
*p = 0.057; ***p < 0.0001 versus placebo (log-rank test stratified by patient type and region)

†p = 0.031 for risperidone LAI versus placebo (log-rank test stratified by region only [adjusted analysis])

Fig. 2. Time to recurrence of any mood episode (primary outcome).

Esketamine demonstrated efficacy in patients with TRD, starting as early as 24 hours (acute study; N = 227)^a

MADRS total score LS mean change from baseline to endpoint (MMRM)

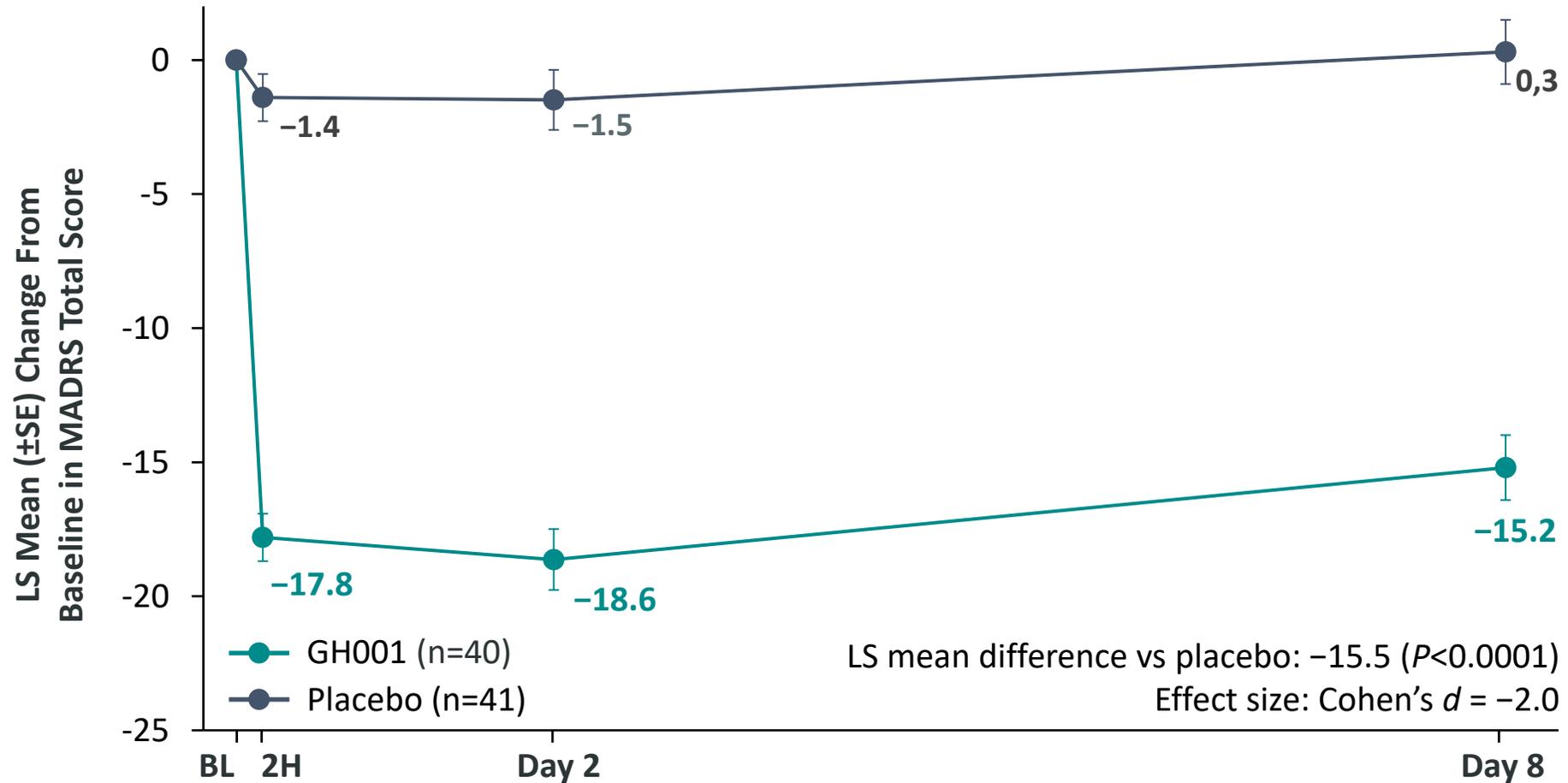


Response and remission rates at Day 28

	ESK + AD	PBO + AD
Remitters	52.5%	31.0%
Responders	69.3%	52.0%

^aTotal number of patients that were randomized. ^bTwo-sided P value.
 CI, confidence interval; ESK, esketamine; LS, least squares; MADRS, Montgomery-Åsberg Depression Rating Scale; MMRM, mixed-effects model using repeated measures; PBO, placebo; SE, standard error.

Mebufotenin (GH001) versus placebo in TRD



Kubala et al, ECNP 2025

Psilocybin in Treatment-Resistant Depression

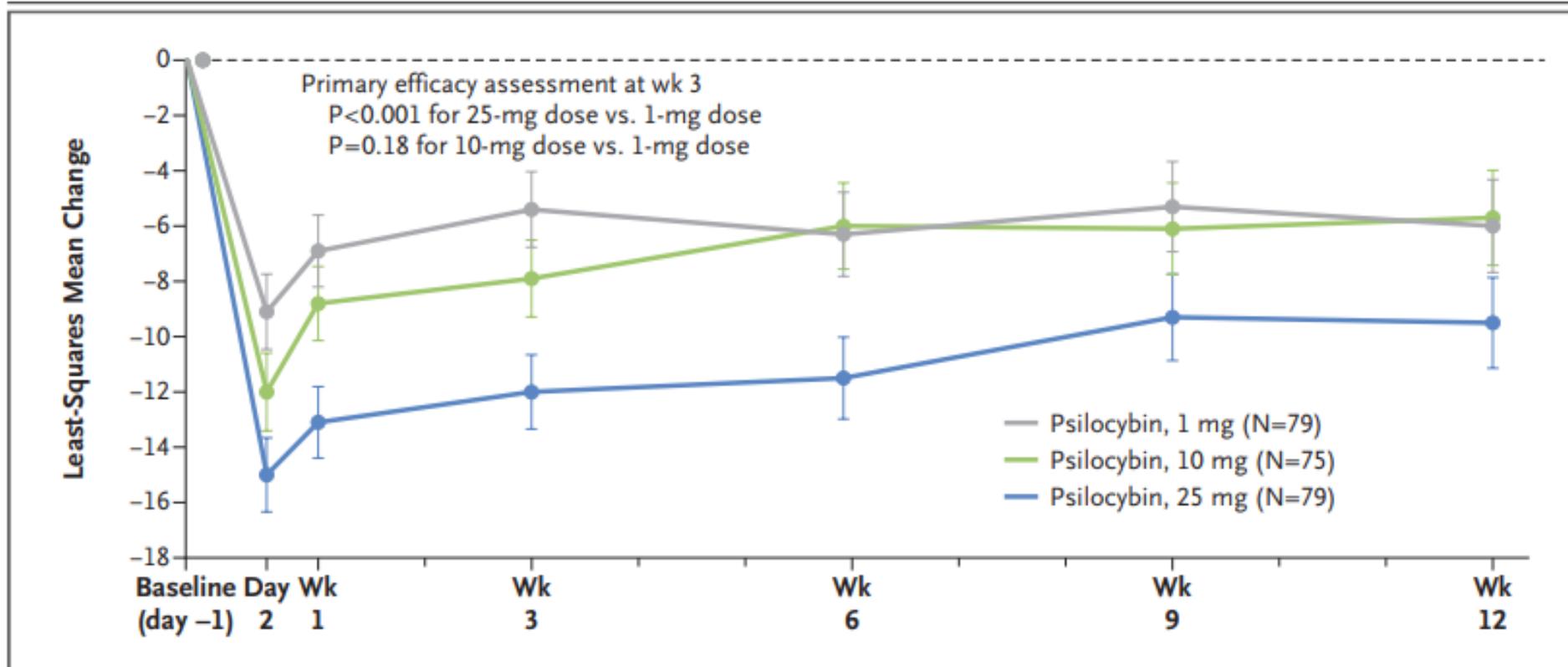


Figure 2. Change from Baseline in MADRS Total Score (Modified Intention-to-Treat Population).

Total scores on the Montgomery-Åsberg Depression Rating Scale (MADRS) range from 0 to 60, with higher scores indicating greater severity of depression. I bars represent standard errors.

Conclusions

- Clinical trials are experimental tests
- They have to meet ethical standards
- There is no such thing as “the perfect trial”
- Look into generalizability, biases, and flaws
- Conflicts of interest are informative but should not raise prejudice
- Most trials are designed to address regulatory demands, not to answer clinical questions

