Psych Congress REGIONALS | VIRTUAL SERIES

Bipolar Disorder Across the Spectrum: *Novel Screening Tools and Treatment Options*

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Faculty Disclosure

- **Dr. Goldberg:** Consultant—BioXcel, Lundbeck, Medscape, Otsuka, Sage Pharmaceuticals, Sunovion, WebMD; Royalties—American Psychiatric Association Publishing, Inc., Cambridge University Press; Speakers Bureau—Allergan, Intracellular Therapies, Otsuka, Sunovion.

- **Dr. Matthews-Hayes**: Speaker—Allergan, AbbVie, Otsuka, Neurocrine, Myriad Neuroscience/Genesight; Advisory Board/Consultant—Allergan (now AbbVie), Neurocrine; Advisor/Ambassador—Allergan (AbbVie) NP Psych Navigator Website.

Disclosure

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
  - Dr. Goldberg will be discussing off-label and investigational use of drugs in the presentation and will identify those issues.

- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.

- This activity has been independently reviewed for balance.

Learning Objectives

- Describe tactics to differentiate and identify various symptom domains in bipolar disorder
- Review the benefits and drawbacks of both traditional and newer screening scales used for bipolar identification
- Analyze treatment targets for current and emerging bipolar medications and their implications for personalized and comprehensive patient care

Burden of Bipolar Disorder Across the Spectrum

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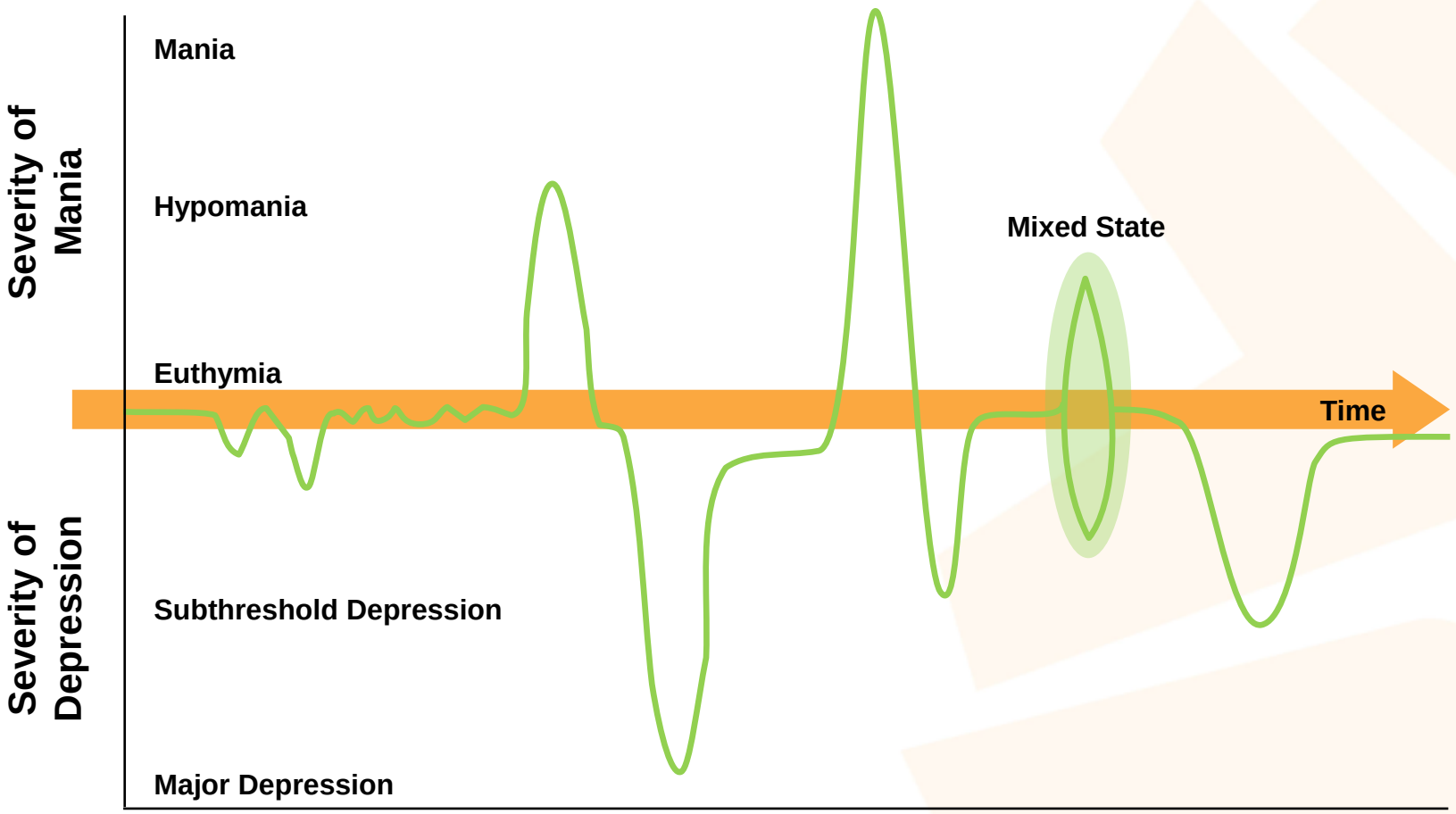
Burden of Bipolar Disorder

Phases of illness



Mania/hypomania:

- High energy/activity essential
- Change from usual baseline
- **Mania (not hypomania)**: can have psychosis, functional impairment

DSM-5 **mixed features** specifier:

- Applies to mania, hypomania, or depression
- A full syndrome + opposite pole subsyndromal features

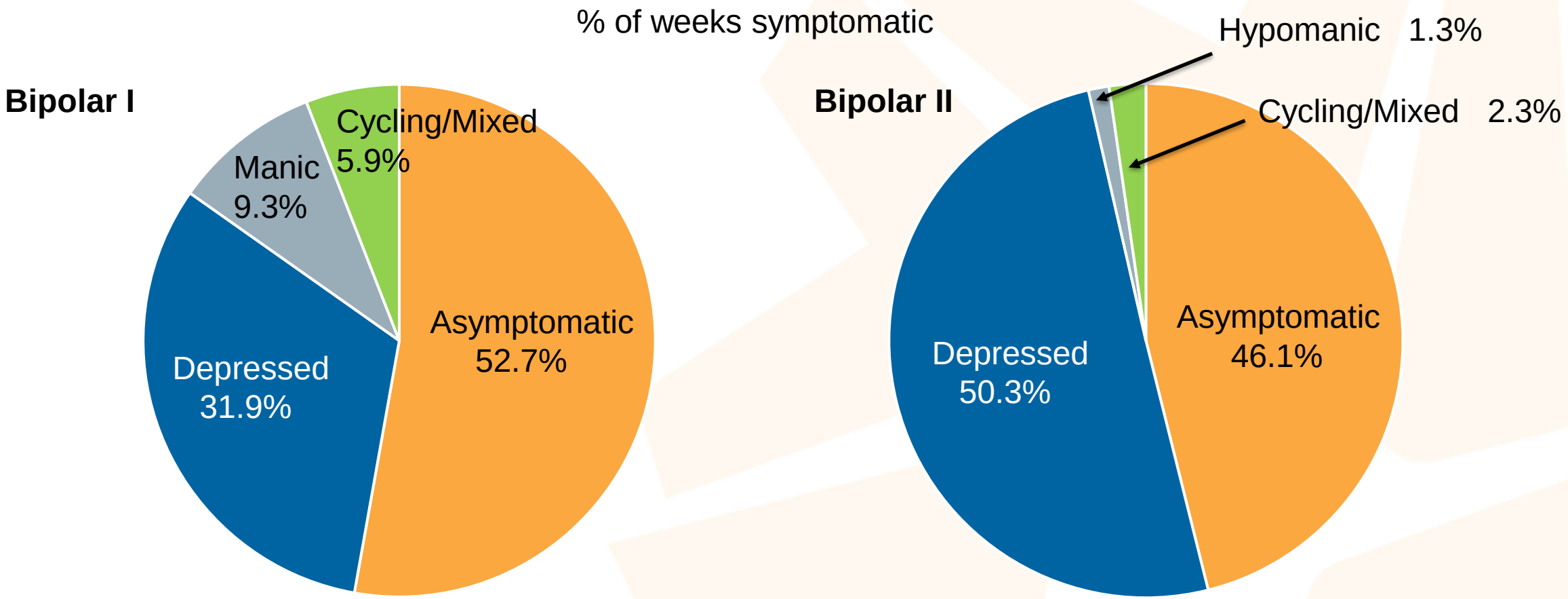
Depressions tend toward

- anergia/atypicality
- prior psychotic depressions
- rejection sensitivity

Grande I, et al. *Lancet*. 2016;387(10027):1561-1572. Mitchell PB, et al. *J Clin Psychiatry*. 2001;62(3):212-216. Ehnvall A, et al. *Bipolar Disord*. 2014;16(2):190-198.

Time Spent with Affective Symptoms

NIMH Collaborative Depression Study: 13-year follow-up



NIMH = National Institute of Mental Health.

Judd LL, et al. *Arch Gen Psychiatry*. 2002;59(6):530-537. Judd LL, et al. *Arch Gen Psychiatry*. 2003;60(3):261-269.

Residual Affective Symptoms

- **NIMH Collaborative Depression Study**: relapse occurred 3× faster among bipolar patients with residual symptoms
- **STEP-BD**: residual depressive symptoms associated with short time to depressive recurrence; residual manic symptoms associated with shorter time to manic, hypomanic, mixed recurrence
- Greater functional impairment when residual symptoms are present:

	Good Outcome (FAST ≤ 11; n=271)	Poor Outcome (FAST > 11; n=197)	*P*
BDRS	3.9 ± 2.3	5.1 ± 2.2	<.001
YMRS	1.6 ± 1.8	2.1 ± 2.0	.046

BDRS = Bipolar Depression Rating Scale; FAST = Functioning Assessment Short Test; YMRS = Young Mania Rating Scale; STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder.

Judd LL, et al. *Arch Gen Psychiatry*. 2008;65(4):386-394. Perlis RH, et al. *Am J Psychiatry*. 2006;163(2):217-224. Samalin L, et al. *Bipolar Disord*. 2016;18(2):164-173.

Key Learning Point

Patients with bipolar I and bipolar II experience depressive symptoms about 30% and 50% of the time, respectively.

Vanessa

- 30-year-old single white female graphic designer
- Telemedicine consultation with a new psychiatrist
- History of depression since childhood
- Alcohol and cannabis use disorder in college, now sober
- Treated with SSRIs and other antidepressants off and on since college, no clear benefits
- Identifies “spurts” of high energy in between periods of depression
- Use of a screening tool to facilitate and clarify possible past periods of mania or hypomania

SSRI = selective serotonin reuptake inhibitor.

Obstacles to Bipolar Identification

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Bipolar Depression

Diagnosis is often difficult as presentation can overlap with multiple other *DSM-5* diagnoses/criteria

Diagnosis is often delayed, or *unipolar depression* is treated for up to 10 years prior to correct identification of *bipolar depression*

Need increased awareness of social impacts as well as increased suicide rates

Nomenclature (use of an SGA) is noted to have an impact on the choices providers make when making treatment choices

There is avoidance of “stigma” associated with being diagnosed with bipolar disorder when they have previously been told they have *unipolar depression*

SGA = second-generation antipsychotic.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. American Psychiatric Association Publishing; 2013. Scrandis DA. *Nurse Pract*. 2014;39(10):30-37. Cha B, et al. *Psychiatry Investig*. 2009;6(2):96-101. Fritz K, et al. *Bipolar Disord*. 2017;19(5):396-400.

Mania

Manic mood states are often easier for the providers to clinically see as they include abnormally elevated or irritable mood, hyperactivity, grandiose moods or increased self-esteem, decreased need for sleep, racing thoughts, being more talkative than usual, and sometimes psychosis; and last shorter periods of time

Patients with mania present to the clinical appointments rather than depressed states, which typically last longer

Patients with mania, while easier to identify, can be more difficult to treat as they often report feeling “great” or the “best they have” relative to the elevated state of mania and increased energy; Elevation can lead to a resistance to treat – patients “like the energy”

When there is an elevation, there is typically a crash, and providers need to be ready to treat the depressive cycle that often follows

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. American Psychiatric Association Publishing; 2013. Vieta E, et al. *Nat Rev Dis Primers*. 2018;4:18008.

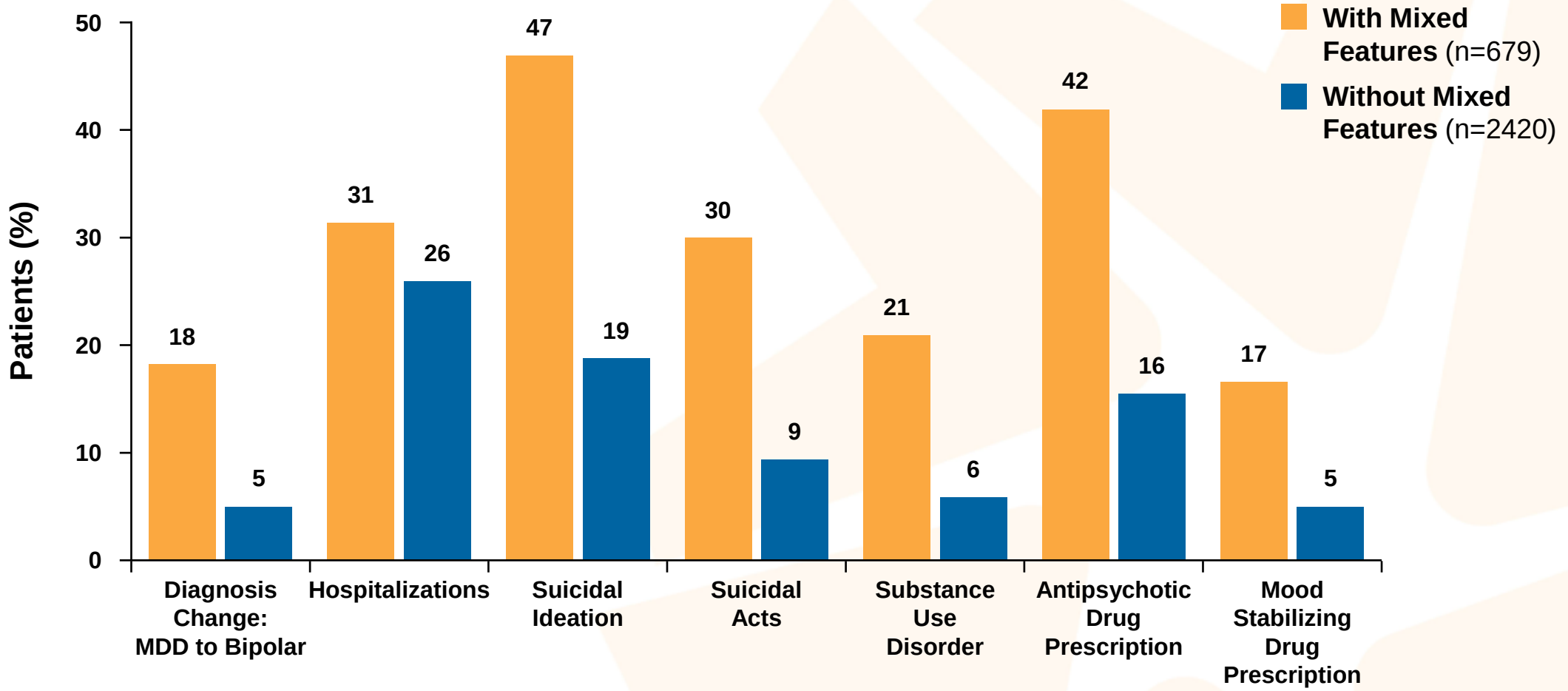
Mixed Features

- Physical presentation can be confusing and often treated as MDD or *unipolar depression*, but can present with mixed features
- Presentation is often misleading or misdiagnosed as many clinical findings support one polarity of mood; however, there are often clinical findings from the opposite polarity
- Delay in correct identification has significant impacts as patients with mixed features have greater rates of hospitalization, substance use disorder, and suicidal ideation when compared to the non-mixed presentation
- Of bipolar states, the mixed presentation would benefit from additional research

MDD = major depressive disorder.

Tondo L, et al. *Acta Psychiatr Scand*. 2018;138(3):243-252. Born C, et al. *BMC Psychiatry*. 2014;14:130.

Comparison of Patients with Mixed Features and without Mixed Features



Tondo L, et al. *Acta Psychiatr Scand*. 2018;138(3):243-252.

Diagnostic Screening Tools in Bipolar Disorder

Mood Disorder Questionnaire

Mood Disorder Questionnaire (MDQ): 13-item self-report measure; scores ≥7 = casehood

Meta-analysis of 23 studies with 6730 participants:

Sensitivity	Specificity	PPV	NPV
61.3%	87.5%	58.0%	88.9%

Better sensitivity for BD-I (66.3%) than BD-II (38.6%)

Operating Characteristics of the Mood Disorder Questionnaire Scored According to Hirschfeld and Colleagues' Algorithm in Studies of the General Population, General Psychiatric Outpatients, and Patients with Mood Disorders

Sample	Number of Studies	n	Prevalence of BD (%)	Sensitivity[a] (%)	Specificity (%)	PPV (%)	NPV (%)
General population	3	1875	5.8	25.9	97.9	43.1	95.6
Psychiatric outpatients	3	943	14.7	64.7	82.3	38.8	93.1
Mood disorder patients	10	2052	39.1	64.7	81.1	68.7	78.2

[a]Sensitivity for all bipolar disorders.
BD-I = bipolar I disorder; BD-II = bipolar II disorder; NPV = negative predictive value; PPV = positive predictive value.
Hirschfeld RM, et al. *Am J Psychiatry*. 2000;157(11):1873-1875. Zimmerman M, et al. *Harv Rev Psychiatry*. 2011;19(5):219-228.

Mood Disorder Questionnaire

Lower MDQ predictive value in mood disorder patients with comorbid substance use disorders

Precision of Self-Rated MDQ(+) Scores for *DSM-IV-TR* Bipolar Diagnoses
Stratified by Any Substances of Abuse or Dependence (N=113)

Substance	n	Sensitivity	Specificity	PPV	NPV
Alcohol	52	0.71	0.47	0.33	0.82
Sedatives	21	0.67	0.28	0.13	0.83
Opiates	25	0.80	0.30	0.22	0.86
Cocaine	24	0.75	0.50	0.23	0.91
Cannabis	34	0.78	0.48	0.35	0.86
Use of > 2 substances	52	0.78	0.42	0.22	0.90
Use of > 3 substances	24	0.60	0.37	0.20	0.78

+ = positive.

Goldberg JF, et al. *J Clin Psychiatry*. 2012;73(12):1525-1530.

Rapid Mood Screener

Rapid Mood Screener Final 6-Item Set (Table View)

Item		Response	
1	Have there been at least 6 different periods of time (at least 2 weeks) when you felt deeply depressed?	Yes	No
2	Did you have problems with depression before the age of 18?	Yes	No
3	Have you ever had to stop or change your antidepressant because it made you highly irritable or hyper?	Yes	No
4	Have you ever had a period of at least 1 week during which you were more talkative than normal with thoughts racing in your head?	Yes	No
5	Have you ever had a period of at least 1 week during which you felt any of the following: unusually happy; unusually outgoing; or unusually energetic?	Yes	No
6	Have you ever had a period of at least 1 week during which you needed much less sleep than usual?	Yes	No

Screener Tool	Concordance Index	Sensitivity	Specificity	PPV	NPV	Accuracy
RMS	0.87	0.88	0.80	0.80	0.88	83.61
MDQ	0.82	0.86	0.78	0.78	0.86	81.97

McIntyre RS, et al. *Curr Med Res Opin*. 2021;37(1):135-144.

Bipolarity Index:
Corroborators of a Suspected Bipolar Diagnosis

	Points	Most points for
Episode characteristics	Up to 20	*DSM-5* mania, fewer for hypomania
Family history	Up to 20	First-degree relatives
Age at onset of depression	Up to 20	Ages 15–19; fewer for earlier or later
Course of illness	Up to 20	Highly recurrent episodes
Response to treatment	Up to 20	Recovery with a mood stabilizer or manic switch with an antidepressant; possible loss of antidepressant response; very rapid antidepressant response

Cut-off score = **50**; sensitivity = 0.91, specificity = 0.90

Aiken CB, et al. *J Affect Disord*. 2015;177:59-64.

Key Learning Point

BD-I is often misdiagnosed as MDD. The reliability of the MDQ self-assessment screening tool may be confounded by current or past substance abuse. The Rapid Mood Screener is a novel, pragmatic, 6-item screening tool designed to help differentiate the two conditions and determine whether the patient should undergo a more comprehensive assessment for BD-I.

Treatment of Bipolar Disorder:
Critical Updates

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Traditional vs Novel and Emerging Treatments

Traditional:

Mood stabilizers

Antidepressants

Antipsychotics

Emerging:

Polarity-specific mood stabilizing properties of drugs

Anticonvulsants do not demonstrate class effects for mood stabilization

Monoaminergic antidepressants: no demonstrated efficacy in bipolar depression

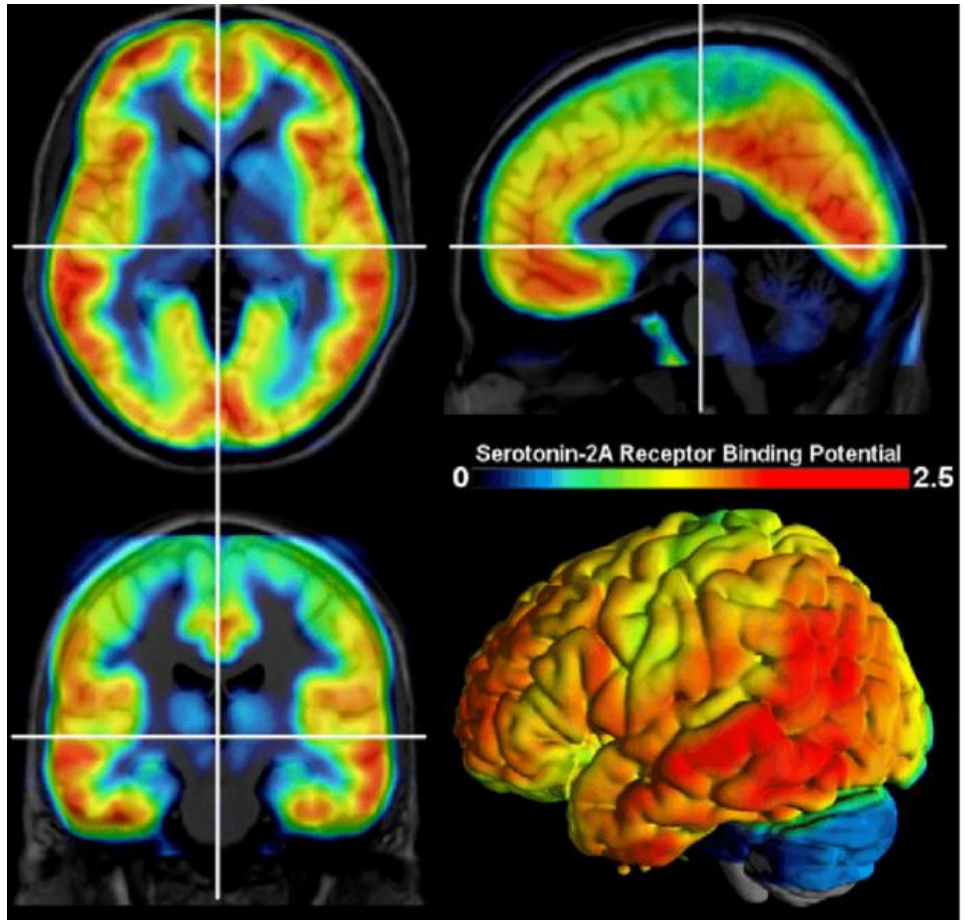
Some (not all) SGAs demonstrate antidepressant value, utility in mania

Novel/off-label agents: ketamine, modafinil, pramipexole, neuroprotective compounds (NAC, omega-3 fatty acids), neuromodulation (rTMS, VNS)

NAC = N-acetylcysteine; rTMS = repetitive transcranial magnetic stimulation; VNS = vagus nerve stimulation.

Mechanisms of Action of Atypical Antipsychotics: Beyond D_2 Blockade

5-HT_{2A} antagonism



Agent	Ki (nM)
Asenapine*	0.06
Ziprasidone*	0.08–1.4
Pimavanserin*	0.087
Risperidone*	0.17
Brexpiprazole*	0.47
Lumateperone*	0.54
Paliperidone*	1.1
Olanzapine*	1.34–24.2
Lurasidone	2.03
Aripiprazole*	3.4–35.0
Clozapine*	9.15
Quetiapine	96–101

Agent	5-HT_{2A} : D_2 Ratio
Risperidone*	11
Olanzapine*	12
Clozapine*	20
Lumateperone*	60

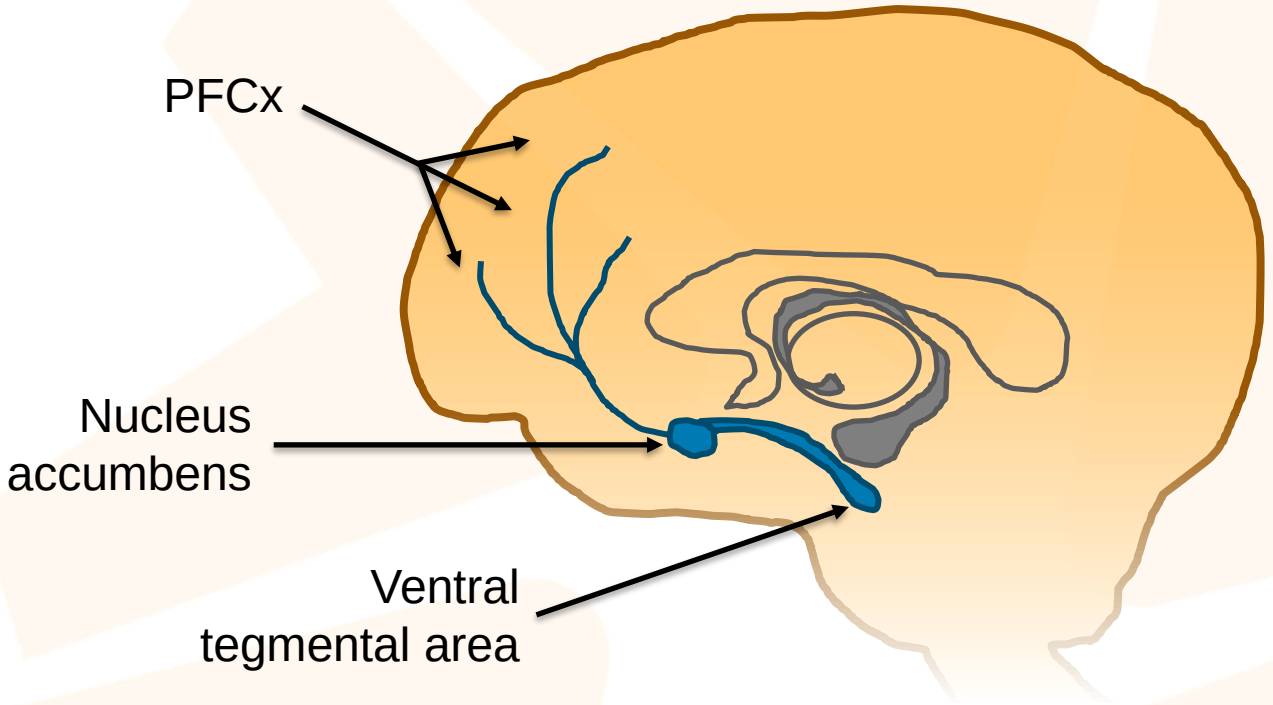
***Not FDA-approved in bipolar depression.**

Herth MH, et al. PET Imaging of the 5-HT_{2A} Receptor System: A Tool to Study the Receptor's In Vivo Brain Function. In: Guiard BP, et al., eds. *5-HT_{2A} Receptors in the Central Nervous System*. Human Press; 2018:85-134. Goldberg JF, et al. *Practical Psychopharmacology: Translating Findings From Evidence-Based Trials into Real-World Clinical Practice*. Cambridge University Press; 2021. Schotte A, et al. *Psychopharmacology*. 1996;124(1-2):57-73.

Mechanisms of Action of Atypical Antipsychotic Drugs

D_2 / D_3 Partial Agonists

Agent	D_3 Ki (nM)
Cariprazine	0.085
Aripiprazole*	0.8–9.7
Brexpiprazole*	1.1
Paliperidone*	3.5
Risperidone*	3.6
Iloperidone*	7.1
Ziprasidone*	7.2
Asenapine*	9.4
Lurasidone	15.7

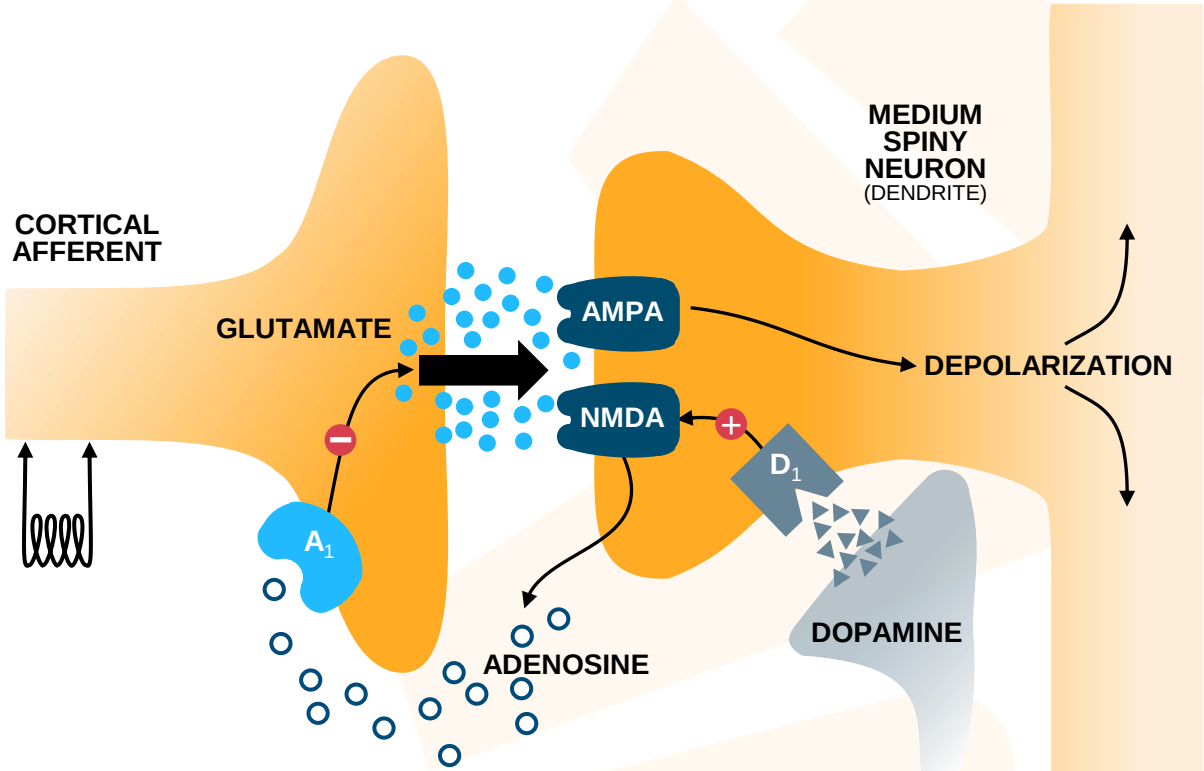


***Not FDA-approved in bipolar depression.**

Goldberg JF, et al. *Practical Psychopharmacology: Translating Findings From Evidence-Based Trials into Real-World Clinical Practice*. Cambridge University Press; 2021.

D_1 Indirect Modulation of Glutamate Function

Agent	Ki (nM)
Asenapine*	8.9
Ziprasidone*	30–130
Olanzapine*	35–118
Lumateperone*	41
Brexpiprazole*	160
Aripiprazole*	265–1170
Clozapine*	266
Quetiapine	712



D_1 postsynaptic receptors modulate presynaptic glutamate release and amplify current caused by activation of NMDA receptors

***Not FDA-approved in bipolar depression.**
AMPA = α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; NMDA = N-Methyl-D-aspartate.
Harvey J, et al. *J Neurosci*. 1997;17(14):5271-5280.

Pharmacologic Treatment Approaches for Bipolar Disorder: *Basic Concepts*

In manic/mixed episodes:

- ✓ Eliminate antidepressants
- ✓ Optimized dosing of antimanic mood stabilizers (lithium levels ~1.0–1.02 mEq/L; valproate levels 70–120 µg/L)
- ✓ Restore normal sleep-wake cycle

In depressive episodes:

- ✓ Favor FDA-approved medications (lurasidone, cariprazine, quetiapine, olanzapine-fluoxetine combination)
- ✓ Other evidence-based pharmacotherapies: lumateperone*, modafinil*, pramipexole*, ketamine*, NAC*, omega-3 fatty acids*; ECT

In maintenance phase:

- ✓ Favor evidence-based interventions (eg, lithium, lithium + divalproex > divalproex, some SGAs)
- ✓ Assure adherence
- ✓ Balance tolerability with efficacy

***Not FDA-approved in bipolar depression.**
ECT = electroconvulsive therapy.

Clinical Profiling

When to Use Antidepressants

Favors Antidepressant Use	Discourages Antidepressant Use
BD-II	BD-I
Pure depressed episodes	Mixed features
Absence of rapid cycling	Past year rapid cycling
Absence of recent mania/hypomania	Mania/hypomania in past 2–3 months
Absence of comorbid alcohol/substance use disorders	Alcohol or substance use comorbidity
Prior favorable antidepressant response	Suboptimal responses to prior antidepressants
No history of antidepressant-induced mania	History of antidepressant-induced mania/hypomania
SLC6A4 “l/l” genotype	*SLC6A4* “s/s” genotype

Goldberg JF. Determining Patient Candidacy for Antidepressant Use in Bipolar Disorder. *Psychiatric Annals*. 2019;49(9):386-391.

Clinical Profiling

When to Use Lithium

- First (few) episode(s)
- + family history of lithium responsivity (67% concordance)
- Mania-prone > depression prone
- Pure euphoric > mixed features
- Absence of rapid cycling
- Absence of comorbid substance use disorders
- History of suicide attempt (though divalproex may be noninferior)

Goldberg JF, et al. *Practical Psychopharmacology: Translating Findings From Evidence-Based Trials into Real-World Clinical Practice*. Cambridge University Press; 2021.

Clinical Profiling

When to Use Divalproex or Carbamazepine

- Multi-episode presentations
- Mania-prone > depression prone
- Mixed or pure manias
- Impulsivity/aggression
- Presence or absence of rapid cycling
- Presence or absence of comorbid alcohol/substance use disorders
- Avoid in sexually active women of reproductive potential

Goldberg JF, et al. *Practical Psychopharmacology: Translating Findings From Evidence-Based Trials into Real-World Clinical Practice*. Cambridge University Press; 2021.

Approaches to Maintenance Therapy
Mood Stabilizers

Mood Stabilizers	Efficacy
Lithium	Prevents mania > depression
Divalproex	Failed maintenance trial; but post hoc analysis found preventive efficacy if enriched for divalproex acute antimanic response
Lithium + Divalproex	BALANCE Trial: Lithium + divalproex > divalproex monotherapy (but not superior to lithium monotherapy)
Carbamazepine	No data
Lamotrigine	Prevention of depression > mania in BD-I; lamotrigine + divalproex no better than lamotrigine monotherapy

Geddes JR, et al. *Am J Psychiatry*. 2004;161(2):217-222. Bowden CL, et al. *Arch Gen Psychiatry*. 2000;57(5):481-489. McElroy SL, et al. *J Affect Disord*. 2008;107(1-3):127-133. BALANCE investigators and collaborators, Geddes JR, et al. *Lancet*. 2010;375(9712):385-395. Goodwin GM, et al. *J Clin Psychiatry*. 2004;65(3):432-441. Bowden CL, et al. *Acta Psychiatr Scand*. 2012;126(5):342-350.

Approaches to Maintenance Therapy
Second-Generation Antipsychotics

SGAs	Efficacy
Aripiprazole	Oral or LAI prevention of mania but not depression
Asenapine	1 (+) 26-week maintenance trial; prevented mania or depression
Lurasidone	1 (-) 28-week maintenance trial
Olanzapine	3 (+) RCTs (vs placebo, lithium, or divalproex)
Quetiapine	2 (+) adjunctive trials, comparable prevention of mania or depression
Risperidone	LAI (prevention of mania but not depression)
Ziprasidone	1 (+) adjunctive trial

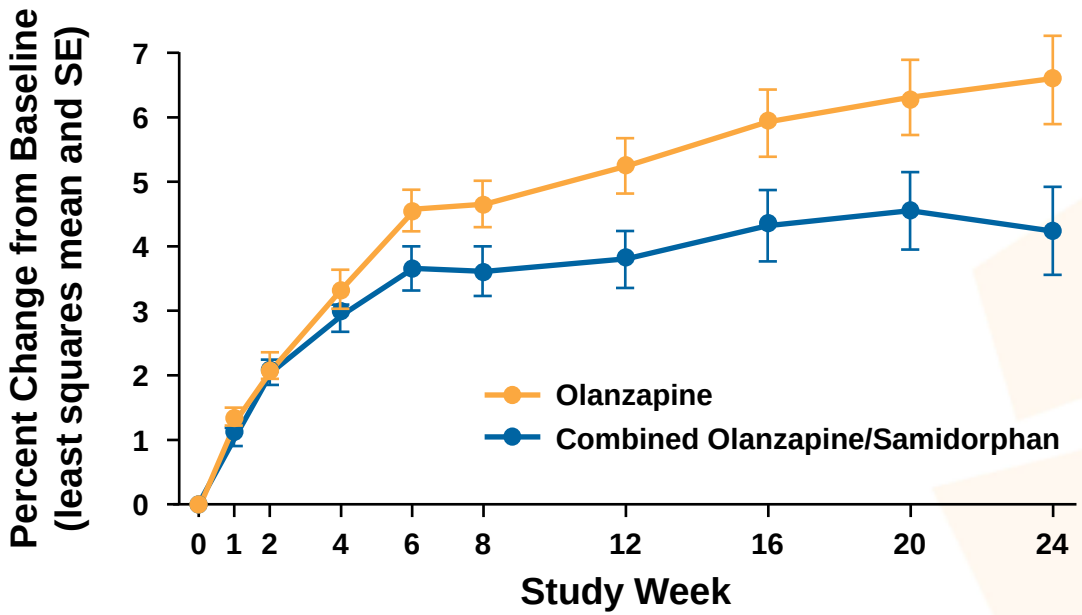
LAI = long-acting injectable; RCT = randomized controlled trial.

Keck PE Jr, et al. *J Clin Psychiatry*. 2007;68(10):1480-1491. Keck PE, et al. *J Affect Disord*. 2009;112(1-3):36-49. Calabrese JR, et al. *J Clin Psychiatry*. 2017;78(3):324-331. Szegedi A, et al. *Am J Psychiatry*. 2018;175(1):71-79. Calabrese JR, et al. *Eur Neuropsychopharmacol*. 2017;27(9):865-876. Tohen M, et al. *Am J Psychiatry*. 2006;163(2):247-256. Tohen M, et al. *Am J Psychiatry*. 2005;162(7):1281-1290. Suppes T, et al. *Depress Anxiety*. 2013;30(11):1089-1098. Quiroz JA, et al. *Biol Psychiatry*. 2010;68(2):156-162. Bowden CL, et al. *J Clin Psychiatry*. 2010;71(2):130-137.

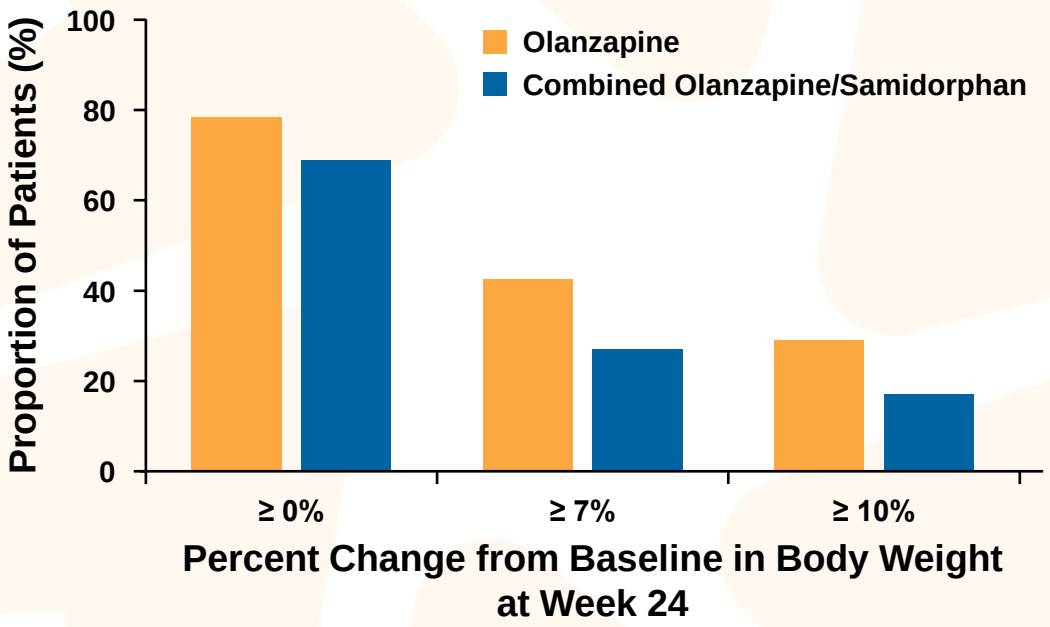
Olanzapine + Samidorphan in Bipolar I Manic/Mixed Episodes

- Samidorphan (10 mg) = μ opiate receptor (MOR) antagonist structurally related to naltrexone + olanzapine 5 mg, 10 mg, 15 mg, or 20 mg
- Current data demonstrate attenuated weight gain in schizophrenia

Least Squares Mean of Percent Change from Baseline in Body Weight by Visit



Proportion of Patients with Weight Changes at Week 24



Correll CU, et al. *Am J Psychiatry*. 2020;177(12):1168-1178.

Neuromodulation in Bipolar Depression

VNS*

- Rationale: vagal nerve afferent fibers enervate brain nuclei
- Not a fast treatment! Separation from placebo only by about 9–12 months

rTMS*

- 14 randomized trials, 50.3% crude response rate compared to 32.5% sham controls; NNT=5.6)

ECT

- Treats either phase of bipolar disorder
- Transient anterograde amnesia but cognitive symptoms of depression improve with ECT
- Safety in pregnancy

***Not FDA-approved in bipolar depression. NNT = number needed to treat.**

McAllister-Williams RH, et al. *Int J Bipolar Disord*. 2020;8(1):13. Nguyen TD, et al. *J Affect Disord*. 2021;279:250-255. Biedermann SV, et al. *Acta Psychiatr Scand*. 2016;134(6):461-468.

Emerging and Novel Pharmacotherapies for Bipolar Depression

- **(Ar)modafinil***: pooled analysis of 2 randomized trials, ES=-0.30
- **Pramipexole***: pooled analysis of 2 studies; ES=4.12 (response)
- Anti-inflammatory agents:
  - **NAC***: 1–2 g/day, ES=-0.75
  - **Omega-3 fatty acids***: 1–6 g/day, ES=-0.36
- **Ketamine***: 3 randomized trials in bipolar depression:

Authors	N	Day 3–4 Response (OR, 95% CI)
Murrough et al.	24	**4.67 (1.57–13.84)**
Diazgranados et al.	18	15.55 (0.70–346.72)
Zarate et al.	15	3.92 (0.14–112.90)

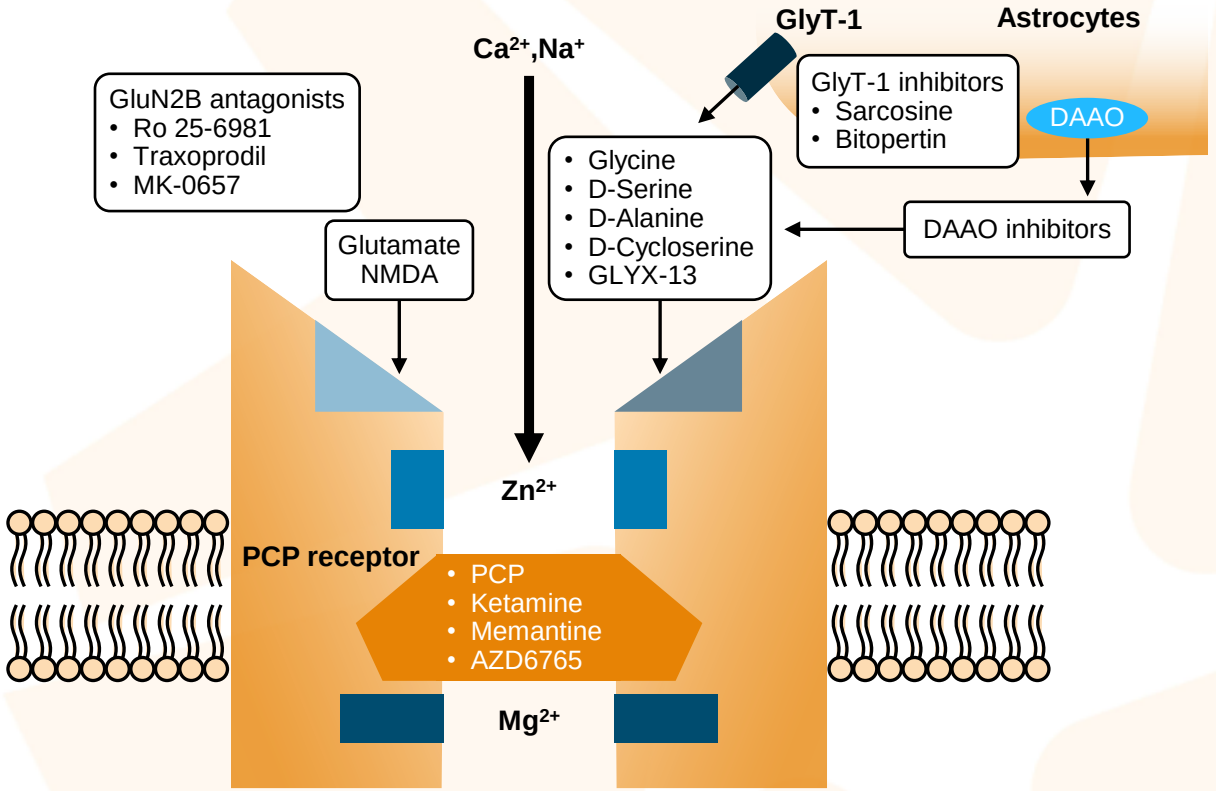
***Not FDA-approved in bipolar depression.**

Goss AJ, et al. *J Clin Psychiatry*. 2013;74(11):1101-1107. Tundo A, et al. *Acta Psychiatr Scand*. 2019;140(2):116-125. Rosenblat JD, et al. *Bipolar Disord*. 2016;18(2):89-101. Murrough JW, et al. *Psychol Med*. 2015;45(16):3571-3580. Diazgranados N, et al. *Arch Gen Psychiatry*. 2010;67(8):793-802. Zarate CA Jr, et al. *Biol Psychiatry*. 2012;71(11):939-946.

NRX-101

- Fixed-dose combination of lurasidone plus D-cycloserine (putative NMDA antagonist believed to increase glutamate/glutamine (Glx) at the glycine site, with activity in the anterior cingulate cortex)

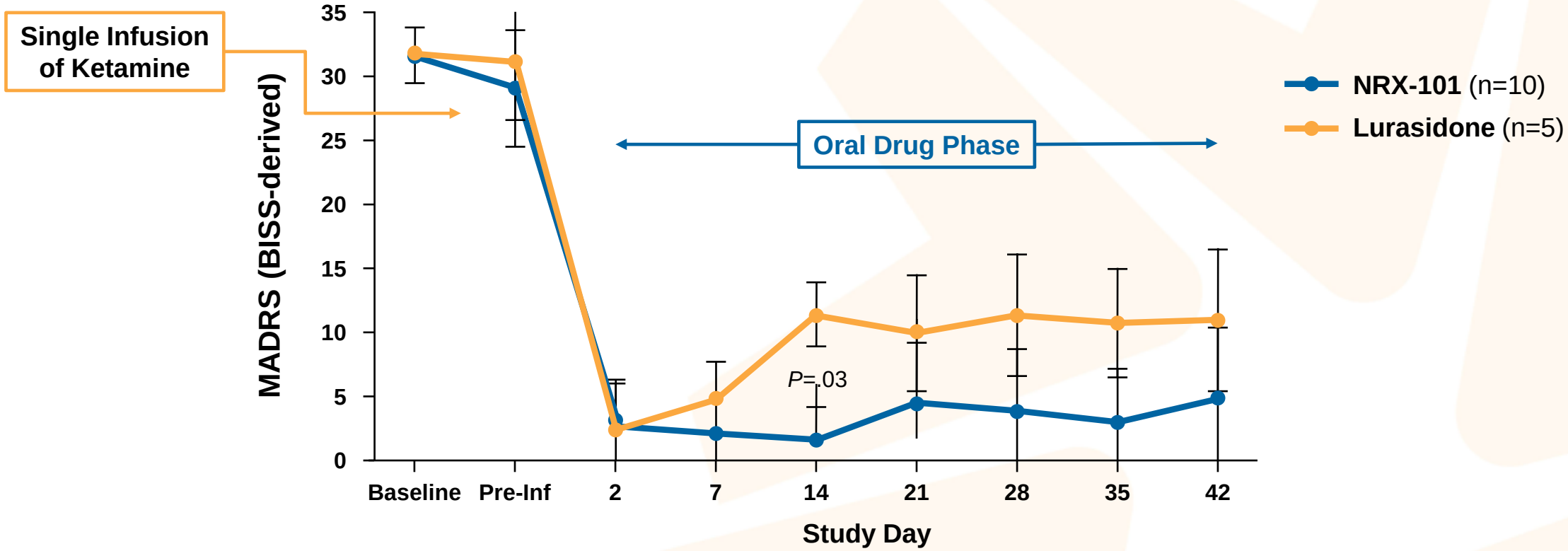
Under Phase 2b/3 investigation as a maintenance therapy after acute response to IV ketamine in bipolar depression as compared to lurasidone monotherapy



Hashimoto K, et al. *Eur Arch Psychiatry Clin Neurosci*. 2013;263(5):367-377. ClinicalTrials.gov Identifier: NCT03396068.

NRX-101
Proof-of-Concept Clinical Data

Depression Score NRX-101 vs Lurasidone

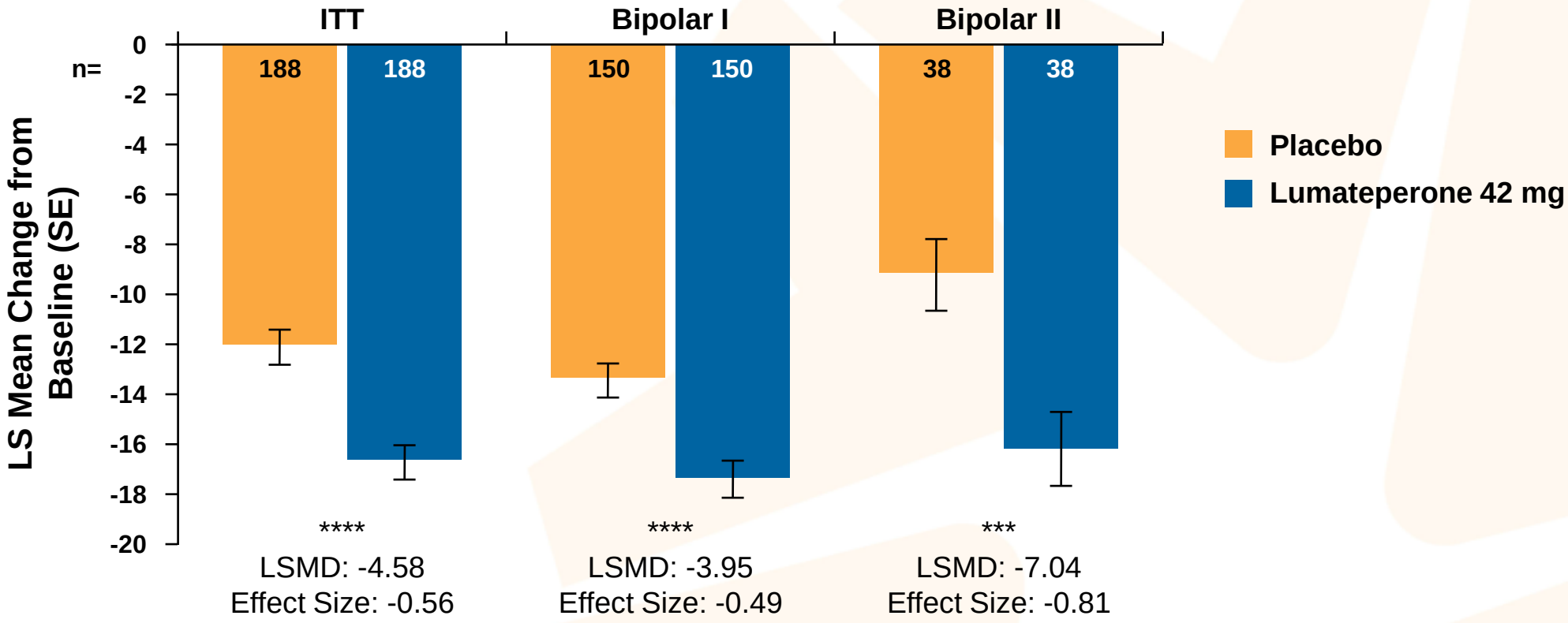


Mixed model to day 42: *P*=.059

BISS = Bipolar Inventory of Symptoms Scale; MADRS = Montgomery–Åsberg Depression Rating Scale.
ClinicalTrials.gov Identifier: NCT02974010.

Lumateperone in Bipolar I and II Depression

LS Mean Change from Baseline to Day 43 in MADRS Total Score



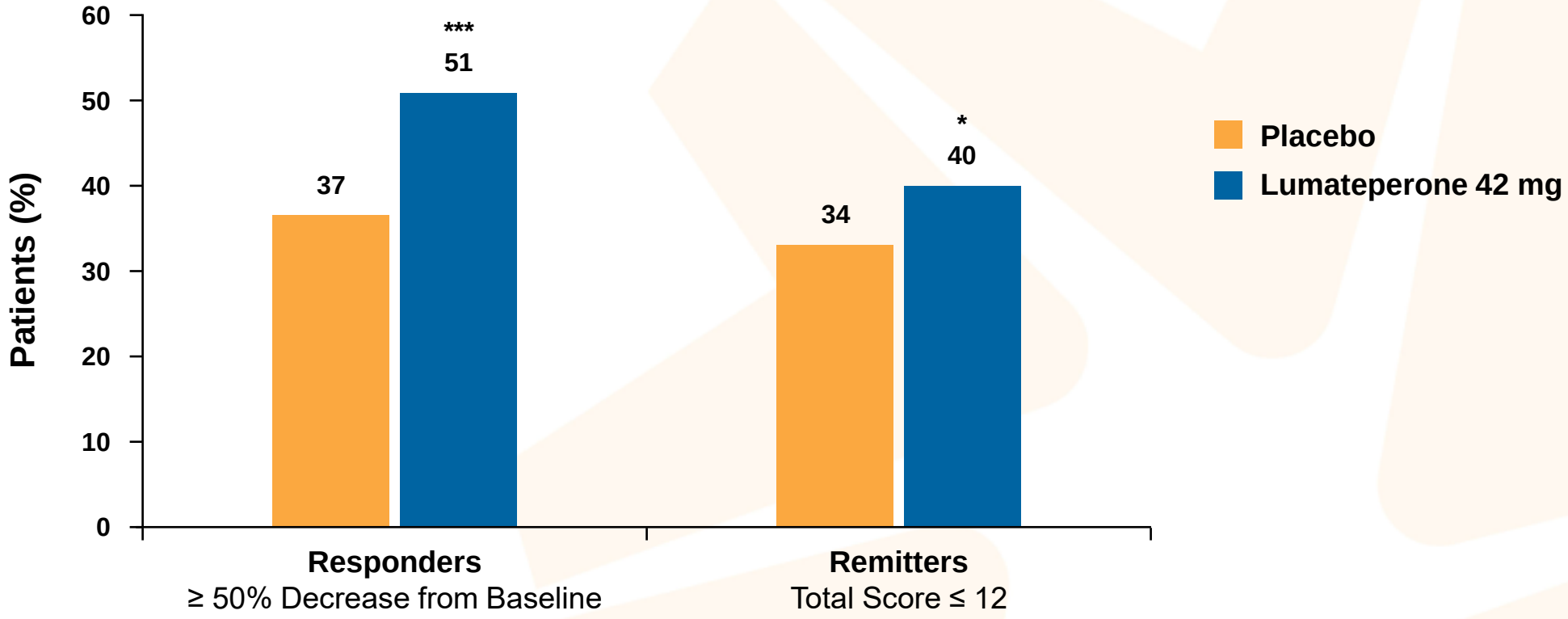
***P<.001, ****P<.0001 LSMD vs placebo.

MMRM. Effect size calculated as LSMD/pooled estimate of within subject error standard deviation.
ITT = intent-to-treat; LS = least squares; LSMD = least squares mean difference; MMRM = mixed-effects model for repeated measures; SE = standard error.

D'Souza I, et al. Efficacy and Safety of Lumateperone (ITI-007) in the Treatment of Depressive Episodes Associated with Bipolar I and II Disorders. Presented at: 2020 Psych Congress Virtual Experience; September 10–13, 2020.

Lumateperone

MADRS Response and Remission at Day 43 in the ITT



***P*<.05, ****P*<.001 vs placebo in the ITT population. Responder and remitter analyses based on logistic regression analysis with terms for site, treatment, and the bipolar disorder stratification at screening.

D'Souza I, et al. Efficacy and Safety of Lumateperone (ITI-007) in the Treatment of Depressive Episodes Associated with Bipolar I and II Disorders. Presented at: 2020 Psych Congress Virtual Experience; September 10–13, 2020.

Key Learning Point

Several emerging and novel agents are in different phases of clinical development for bipolar depression, including NRX-101 and lumateperone. A recent Phase 3 randomized, double-blind, placebo-controlled trial of lumateperone found improvement in MADRS scores in patients with depressive episodes associated with bipolar I and II disorders.

Vanessa

- Clinical history suggests past high periods and poor efficacy with antidepressants
- Comprehensive care plan involves
  - psychoeducation about bipolar disorder,
  - lifestyle factors including risk for mood worsening with alcohol and substance use,
  - introduction of an evidence-based treatment for bipolar depression,
  - symptom reassessment, and
  - role for ongoing comprehensive care including pharmacology and psychotherapy

Take-Home Messages

- Use rating scales as initial screens for bipolar disorder; not proxies for diagnosis
- Recognize corroborative features for ruling in or out diagnoses of bipolar disorder
- Consider within-class differences among “mood stabilizers” and SGAs in demonstrated antimanic vs antidepressant efficacy
- Recognize potential breadth of mechanisms of action among SGAs (involving serotonergic and dopaminergic effects, among others) that may contribute to efficacy in bipolar depression for at least some agents
- Emerging role for novel pharmacotherapies and forms of neuromodulation targeting bipolar depression

Q&A