Introduction: This study is about the clinical uses of three antidepressants(escitalopram, desvenlafaxine, vortioxetine) in the treatment of anxioun depression.
Objectives: The purpose of this study was to compare the efficacy and safety of escitalopram, desvenlafaxine, vortioxetine, and aripiprazole augmentation with escitalopram in the acute treatment of anxious depression.
Methods: Patients (n=189) with DSM5 major depression and high levels of anxiety were evenly randomized to escitalopram, desvenlafaxine, vortioxetine, and aripiprazole augmentation with escitalopram in a six-week, randomized, rater-blinded, head to head comparative trial. Changes in overall depressive and anxiety symptoms were assessed.
Results: Patients demonstrated similar baseline-to-endpoint improvement in HAMD and HAMA total scores. Patients also demonstrated similar response rate and remission rate in HAMD and HAMA. In analysis of individual HAMD and HAMA items, desvenlafaxine had greatly reduced scores for anxiety somatic (p=0.013), hypochondriasis (p=0.014), cardiovascular symptoms (p=0.005), respiratory symptoms (p=0.013) compared to escitalopram or vortioxetine. Each treatment were well tolerated with no significant differences.
Conclusions: These results showed no significant differences in efficacy and tolerability of escitalopram, desvenlafaxine, vortioxetine, and aripiprazole augmentation with escitalopram in this subtype of patients with anxious depression during the acute phase treatment.

Disclosure: No significant relationships.
Keywords: escitalopram; desvenlafaxine; Depression; vortioxetine

O0091

Clinical Efficacy of a 2-Week Treatment Course of Zuranolone for the Treatment of Major Depressive Disorder and Postpartum Depression: Outcomes From the Clinical Development Program

A. Clayton[1]*, A.J. Cutler[2], K.M. Deligiannidis[3], R. Lasser[4], A. J. Sankoh[5], J. Doherty[4] and M. Kotecha[6]

[1]University of Virginia School of Medicine, Department Of Psychiatry And Neurobehavioral Sciences, Charlottesville, United States of America; [2]SUNY Upstate Medical University, Department Of Psychiatry, Syracuse, United States of America; [3]Zucker Hillside Hospital, Department Of Psychiatry, Glen Oaks, United States of America; [4]Sage Therapeutics, Inc, Clinical Development, Cambridge, United States of America; [5]Sage Therapeutics, Inc, Data Science, Cambridge, United States of America and [6]Biogen, Clinical Development, Cambridge, United States of America
*Corresponding author.
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Introduction: Antidepressants that offer a rapid onset of action without requiring chronic use are greatly needed in both major depressive disorder (MDD) and postpartum depression (PPD). Zuranolone is an investigational, oral, neuroactive steroid and $GABA_A$ receptor positive allosteric modulator in clinical development as a 2-week treatment course for MDD and PPD.
Objectives: To present the efficacy and safety of zuranolone vs placebo in Phase 2 and 3 trials.
Methods: In the studies presented (**Table 1**), improvements in depressive symptoms were assessed by least-squares mean (LSM) using a mixed-effects model for repeated measures on the change from baseline (CFB) at Day 15 in the 17-item Hamilton Rating Scale for Depression total score (HAMD-17; primary endpoint for all trials) and the Montgomery–Åsberg Depression Rating Scale (MADRS; secondary endpoint) following a 14-day treatment course of once-daily zuranolone.

Table 1. Completed Placebo-Controlled Zuranolone Trials: Design and Inclusion Criteria

	MDD-201B (NCT03000530) N=89[a]	MOUNTAIN (NCT03672175) N=570[a]	WATERFALL (NCT04442490) N=537[a]	ROBIN (NCT02978326) N=151[a]
Indication	MDD	MDD	MDD	PPD
Phase	2	3	3	3
Zuranolone dose, mg	30	20 or 30	50	30
Baseline HAMD-17 score	≥22	≥22	≥24	≥26
Baseline MADRS score	≥32	≥32	≥32	≥28

HAMD-17, 17-item Hamilton Rating Scale for Depression; MADRS, Montgomery–Åsberg Depression Rating Scale; MDD, major depressive disorder; PPD, postpartum depression. [a]Safety set.

Results: Compared with placebo, zuranolone treatment led to rapid improvements in depressive symptoms across clinical trials, with significant improvements (LSM treatment difference [SE] in CFB) in HAMD-17 and MADRS scores at Day 15 in 3 of the 4 trials (**Table 2**). Common treatment-emergent adverse events (≥5% in zuranolone treatment arms) were headache, somnolence, dizziness, nausea, sedation, diarrhea, upper respiratory tract infection, and fatigue (**Table 3**). No incidences of loss of consciousness or excessive sedation were observed.

Table 2. Treatment Difference (Zuranolone – Placebo) in HAMD-17 and MADRS Scores (CFB at Day 15): Efficacy Analysis Set

	MDD-201B (NCT03000530) N=89	MOUNTAIN[b] (NCT03672175) N=482[c]	WATERFALL (NCT04442490) N=534[d]	ROBIN (NCT02978326) N=150
LSMD (SE)	ZRN 30 mg	ZRN 30 mg	ZRN 50 mg	ZRN 30 mg
HAMD-17	−7.0 (1.6) p<0.001[a]	−1.4 (0.9) p=0.116	−1.7 (0.7) p=0.014[a]	−4.2 (1.4) p=0.003[a]
MADRS	−7.6 (2.4) p=0.002[a]	−2.0 (1.4) p=0.144	−2.4 (1.1) p=0.024[a]	−4.6 (1.9) p=0.018[a]

CFB, change from baseline; HAMD-17, 17-item Hamilton Rating Scale for Depression; LSMD, least-squares mean treatment difference (zuranolone – placebo); MADRS, Montgomery–Åsberg Depression Rating Scale; ZRN, zuranolone. [a]Statistically significant vs placebo. [b]Zuranolone 20 mg was also assessed in MOUNTAIN; [c]N=446 at Day 15. [d]N=499 at Day 15 (HAMD-17) and N=498 at Day 15 (MADRS).

Table 3. Treatment-Emergent Adverse Events With ≥5% Incidence in Any Zuranolone Treatment Group: Safety Set

	Range of incidence across 4 studies, %[a]	
Preferred term	Placebo	Zuranolone
Headache	0.4-15.9	6.3-17.8
Somnolence	2.3-11.0	5.9-15.4
Dizziness	2.2-5.5	5.7-13.8
Nausea	2.3-8.2	3.6-11.1
Sedation	0-4.5	4.4-7.5
Diarrhea	2.7-6.8	0-6.4
Upper respiratory tract infection	0-1.4	0-8.0
Fatigue	0-2.6	0-6.8

MDD, major depressive disorder; PPD, postpartum depression.
[a]Studies included 3 MDD studies (MDD-201B, NCT03000530; MOUNTAIN, NCT03672175; WATERFALL, NCT04442490) and 1 PPD study (ROBIN, NCT02978326).

Conclusions: Across the completed studies in the zuranolone clinical trial program, patients receiving zuranolone consistently experienced improvement in depressive symptoms following a 2-week treatment course. Treatment with zuranolone was generally well tolerated with a consistent safety and tolerability profile.

Disclosure: The MDD-201B, MOUNTAIN, and ROBIN studies were sponsored by Sage Therapeutics, Inc; the WATERFALL study was sponsored by Sage Therapeutics, Inc, and Biogen. Medical

writing and editorial support were provided by MediTech Media, Ltd, and funded by Biogen.
Keywords: postpartum depression; zuranolone; rapid onset of action; major depressive disorder

O0093

Benzodiazepine use during cariprazine treatment in acute schizophrenia

C. Correll[1]*, B. Sebe[2], R. Csehi[2], K. Acsai[2] and Á. Barabássy[2]
[1]The Zucker Hillside Hospital, Department Of Psychiatry, Glen Oaks, United States of America and [2]Gedeon Richter Plc, Medical Division, Budapest, Hungary
*Corresponding author.
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Introduction: Although antipsychotics are first-line treatments for schizophrenia, benzodiazepines (BZDs) are often used as concomitant medications in acutely exacerbated patients due to their anxiolytic and sedative effects. Cariprazine (CAR), a D3-preferring dopamine D2/D3 partial agonist antipsychotic, has been examined in many clinical studies for the treatment of acute schizophrenia, with and without benzodiazepines.
Objectives: To delineate the effects of benzodiazepine-use during cariprazine treatment in acute schizophrenia.
Methods: Pooled data of cariprazine-treated (1.5-6mg/day) and placebo-treated patients from four short-term, randomised, double-blind trials (NCT00404573, NCT01104766, NCT01104779, NCT00694707) were analysed. Baseline characteristics (age, duration of illness) and efficacy outcome parameters (Total and Hostility Factor Score of the Positive and Negative Syndrome Scale [PANSS]) were compared in patients receiving benzodiazepines (for more ≥3 consecutive days) and not receiving benzodiazepines (<3 consecutive days).
Results: Altogether, 36.7% and 40.7% of the CAR-treated and PBO-treated patients required BZDs. BZD-taking was associated with a higher age in both the CAR-treated ($p=0.0002$) and PBO-treated ($p<0.0001$) patients, and with longer illness-duration in both treatment groups ($p<0.0001$). PANSS Total Score at baseline was similar for BZD users and non-users (CAR: LS Mean=96.36 and 96.27; PBO: LS Mean=95.55 and 96.66). Change from baseline in the PANSS Total Score was greater for patients who did not use BZD vs those who did (CAR: LS Mean= -23.8 vs LS Mean 17.2, $p<0.0001$; PBO: LS Mean= -14.0 vs LS Mean 12.9, $p=0.5776$).
Conclusions: These findings may suggest that requiring benzodiazepines is a potential indicator of longer illness duration and poorer response in acute schizophrenia.

Disclosure: I am an employee of Gedeon Richter Plc.
Keywords: benzodiazepine; cariprazine; schizophrénia; Pharmacotherapy

O0094

Characterising the evolution of antipsychotic polypharmacy and clozapine prescribing patterns in schizophrenia patients during psychiatric hospitalisations

J. Lagreula[1]*, L. Elens[2], P. De Timary[3] and O. Dalleur[4]
[1]Université Catholique de Louvain, Louvain Drug Research Institute (LDRI), Clinical Pharmacy Research Group (clip), Brussels, Belgium; [2]Université Catholique de Louvain, Louvain Drug Research Institute, Integrated Pharmacometrics, Pharmacogenomics And Pharmacokinetics, Brussels, Belgium; [3]Université Catholique de Louvain, Institute Of Neuroscience, Brussels, Belgium and [4]Université Catholique de Louvain, Louvain Drug Research Institute, Clinical Pharmacy Research Group, Brussels, Belgium
*Corresponding author.
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Introduction: A high prevalence of antipsychotic polypharmacy (APP) and low utilisation of clozapine is considered as inappropriate prescribing that can lead to suboptimal treatment, increased risk of poor response or adverse effects.
Objectives: To explore the evolution of prevalence of APP and associated factors as well as clozapine prescribing patterns between hospital admission and discharge.
Methods: We collected retrospective data on adult inpatients diagnosed with schizophrenia spectrum disorders in 2020-2021 in 6 Belgian hospitals.
Results: Of the 516 patients analysed, APP prescribing significantly increased from 47.9% on hospital admission to 59.1% at discharge. Both on admission and at discharge, APP was associated with treatment with a first-generation antipsychotic, not being treated with an antidepressant nor a mood stabilizer, high antipsychotic dosage, increased number of psychoactive cotreatments and total medicines. A lower number of comorbidities (OR=0.68, CI=0.50-0.91), no treatment with benzodiazepines (OR=0.02, CI=0.01-0.09) nor with trazodone or sedative antihistamines (OR=0.06, CI=0.01-0.03) and two or more previous antipsychotic trials (OR=4.91, CI=1.30-18.57) was associated with APP on admission only. APP at discharge was more frequent in patients with antipsychotic adverse effects (OR=2.57, CI=1.10-6.00), prior clozapine use (OR=16.30, CI=3.27-81.22) and not involuntary admitted (OR=0.26 CI=0.08-0.88). Contrary to admission, treatment with benzodiazepines was associated with APP at discharge (OR=10.9, CI=3.38-5.38). Only 9.3% of admitted patients were treated with clozapine. Although 28.1% were eligible, clozapine was introduced to 10 patients leading to 11% being discharged on it.
Conclusions: Inappropriate prescribing of antipsychotics to schizophrenia patients persist after psychiatric hospitalisations and are associated with identifiable characteristics.

Disclosure: No significant relationships.
Keywords: clozapine; Psychiatric hospitalisations; Antipsychotic polypharmacy; Clinical pharmacy

O0095

DNA methylation may mediate psychotropic drug-induced metabolic side effects: results from a 1-month observational study

C. Dubath[1]*, E. Porcu[2], A. Delacrétaz[1], C. Grosu[1], N. Laaboub[1], M. Piras[1], A. Von Gunten[1], P. Conus[1], K. Von Plessen[1], Z. Kutalik[2] and C. Eap[1]
[1]Lausanne University Hospital, Psychiatry, Prilly, Switzerland and [2]Swiss institute of bioinformatics, Bioinformatics, Lausanne, Switzerland
*Corresponding author.
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Introduction: Metabolic side effects of psychotropic medications are a major drawback to patients' effective treatment. Among the