intruder test, reflects decreased aggressive motivation. Behavioral changes in recipients were accompanied with cytokines brain changes: decreased IL-1β, IL-2, IL-6, INFγ in the hippocampus; increased IL-4 and decreased INFγ in the hypothalamus; decreased IL-1β in the frontal cortex.
Conclusions: Chlorpromazine - modulated immune cells have a positive aggressive behavior editing effect being involved in the central mechanisms underlying the development of aggressive reactions.

Disclosure: No significant relationships.
Keywords: aggression; immune cells

O0087

SSRIs treatment did not completely restore affective state in patients with the initial clinically confirmed major depressive disorder/generalized anxiety disorder after COVID-19 disease

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Introduction: The major clinical outcomes of COVID-19 in the brain are associated with its deleterious neurological and mental health actions.
Today, there are limited findings concerning the studying of neuropsychiatric action for SARS-Cov-2 in humans after COVID-19 disease.
Objectives: The aim of the present study was to compare the efficacy of SSRIs (escitalopram, sertraline and fluoxetine) for 6 months therapy on the affective profile of man and women with the clinically confirmed Major Depressive Disorder (MDD) or Generalized Anxiety Disorder (GAD) cases following COVID-19 disease.
Methods: . For the assessment of affective profile in man and women (30-55 years) with the initial clinically confirmed MDD or GAD cases after COVID-19 disease, we used the different tests: Montgomery-Asberg Depression Rating Scale (MADRS) and anxiety scale (ShARS Scale). The hormonal and monoamines levels in the serum blood were measured by ELISA tests before and after SSRIs therapy.
Results: After 6 months of SSRIs therapy, MADRS Scale showed a incomplete disappearance of the depressive/anxiety manifestations in both men and women with the initial clinically confirmed MDD case after COVID-19 ($p<0,05$). We found that SSRIs were able to reduce depression/anxiety levels only on 20% in man or on 30% in women with the initial MDD case after COVID-19 before treatment.
Conclusions: SSRIs treatmet alone failed to produce the decrease of depression/anxiety in the patients of both gender with the initial MDD or GAD diagnosis after COVID-19. The further randomized clinical trials involving new pharmacological therapies for psychiatric pations after COVID-19 disease are needed.

Disclosure: No significant relationships.
Keywords: Covid-19; depression; anxiety; SSRIs; pharmacotherapy

O0089

Clinical, genetic and environmental influences on weight gain and metabolic disorders induced by psychotropic drugs

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Introduction: Weight gain and obesity are important health problems associated with psychiatric disorders and/or with psychotropic drug treatments. There is a high inter-individual variability in the susceptibility to drug induced weight gain and/or other cardiometabolic disorders.
Objectives: To study the genetic and environmental risk factors for weight gain and onset of metabolic syndrome during psychotropic treatment
Methods: Analysis in PsyMetab, a large (n>3000) ongoing longitudinal prospective cohort study investigating cardiometabolic disorders in psychiatric patients.
Results: Aside from well-known clinical risk factors for metabolic worsening (e.g. young age, first episode status, rapid weight gain during the first month of treatment and/or low initial BMI), additional risk factors have been recently identified. We showed an inverse association between socio-economic status (SES) and worsening of cardiometabolic parameters, adult patients with a low SES having a three-fold higher risk of developing metabolic syndrome over one year versus patients with a high SES (n=366). In addition, a causal inverse effect of educational attainment on BMI was revealed using Mendelian randomization in the UKBiobank (n=30'069). Results from an epigenome-wide association study (EWAS) performed in 78 patients before and after one month of treatment and from a genome-wide association study (GWAS) in 1924 patients will also be presented.
Conclusions: Differences in clinical, genetic and environmental factors contribute to the differences in weight gain and metabolic disorders induced by psychotropic drugs. When starting a psychotropic drug at risk, a prospective monitoring of clinical (e.g. weight and blood pressure) and biochemical (fasting glucose, lipid levels) parameters is essential.

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Keywords: Genetics; metabolic syndrome; psychotropic drugs; epigenetics

O0090

Comparative efficacy and safety of escitalopram, desvenlafaxine, and vortioxetine in the acute treatment of anxious depression: A randomized rater-blinded, 6-week clinical trial

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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

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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