- **Cluster 2 (43.1%):** Despite high olanzapine levels (>4.35 μg/L), patients showed poor response, with elevated PANSS negative (24.73 vs. 21.22, $p < 0.001$) and total scores (91.45 vs. 79.88, $p < 0.001$), along with reduced glutamatergic activity in the PCC and ACC.
- **Cluster 3 (35.3%):** Younger patients (mean age: 21.2 years) with normal olanzapine levels but elevated glutamate and glutamine in the cingulate cortex, indicating potential early-stage hyperglutamatergic dysregulation.

Neurochemical correlations showed that glutamate positively correlated with psychotic symptoms ($r = 0.29$, $p = 0.049$), while glutamine correlated negatively ($r = –0.29$, $p = 0.045$). Serotonin correlated with negative symptoms ($r = 0.32$, $p = 0.029$).
Conclusions: This study supports the feasibility of phenotype-driven treatment stratification in schizophrenia.

- **Cluster 1** patients may benefit from lower olanzapine doses.
- **Cluster 2** may require alternative strategies, such as glutamatergic modulation or switching to clozapine.
- **Cluster 3** could benefit from early neurochemical monitoring (e.g., MRS) to prevent progression.

Routine therapeutic drug monitoring (TDM), combined with neurochemical profiling, may improve treatment outcomes and minimize adverse effects in schizophrenia.

Disclosure of Interest: None Declared

EPV1205

Plasma microRNAs reproducibly identify a schizophrenia subgroup characterized by high inflammation, and associate symptom severity with inflammation

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Introduction: Schizophrenia is a complex and heterogeneous psychiatric disorder. Our previous study identified three patient subgroups characterized by different inflammation levels, defined by 40 plasma microRNAs (miRNAs) (Miyano et al. Int J Mol Sci 2024; 25 4291).
Objectives: This study aimed (1) to evaluate the reproducibility of miRNA-based stratification of patients with schizophrenia, and (2) to investigate biological pathways linking symptom scores with inflammation through plasma miRNA analyses.
Methods: Plasma levels of 376 miRNAs and the Positive and Negative Syndrome Scale (PANSS) were obtained in 70 schizophrenia patients. This cohort differed from the previous study in race, symptom phase, medication protocols, and the platform used for miRNA quantification. For aim (1), we examined whether the 40 previously identified miRNAs could classify three subgroups. For aim (2), we developed regression models to determine miRNAs associated with PANSS. miRNA combinations were optimized to minimize cross-validation error. We conducted a systematic literature review to evaluate whether symptom-related miRNAs exert stimulatory or inhibitory effects on pro-inflammatory cytokine expression. The study was approved by the Ethical Research Practice Committee of Daiichi Sankyo Co., Ltd.
Results: The plasma miRNA profiles identified similar subgroups of patients as in the previous study, suggesting miRNA-based patient stratification is potentially reproducible. Development of regression models identified optimal combinations of 32 and 42 miRNAs for estimating the PANSS positive and negative subscales, respectively. Our literature-based survey confirmed that a part of these miRNAs exert either positive or negative effects on IL-1β, IL-6, and TNFα. Integrating the directions of the regression coefficients with the reported effects of these miRNAs on pro-inflammatory cytokines suggests that more severe positive and negative symptoms are associated with higher levels of inflammation.
Conclusions: Plasma miRNAs may serve as robust biomarkers for identifying subgroups with distinct pathophysiological profiles such as inflammation. Our finding suggest that anti-inflammatory interventions may improve positive and negative symptoms in patients with high inflammation.

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EPV1206

Association between blood concentration of sertraline and its effectiveness and safety in major depression: exploratory results of the PREDEP-SERT study

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Introduction: Antidepressant medication is an integral part of the treatment for major depressive disorder (MDD), and selective serotonin reuptake inhibitors (SSRIs) are common first line options. Genetic and environmental factors can lead to toxicity or lack of efficacy within the established dose ranges of SSRIs, requiring the use of lower or higher doses in order to avoid the risk of clinical complications due to toxicity or excessively prolonged response latency. The determination of blood levels by means of therapeutic drug monitoring (TDM) may be determinant in this regard. In the case of sertraline, further evidence is needed regarding the optimal therapeutic range of this drug in MDD.
Objectives: This study aims to assess the optimum ranges of blood concentrations of sertraline associated with therapeutic response and safety, and relevant clinical, demographic and genetic factors.
Methods: The PREDEP-SERT study (PREdictors of response in DEPression treated with SERTraline) is an ongoing, single-center, observational, longitudinal, ambispective cohort study of patients with MDD to investigate the association between blood