

Use Disorders (SUDs), illness duration, or socio-demographic features can interfere with the appraisal of effect of RCU on these symptoms. Studies are rarely adjusted for these variables and no adjustment can be performed in meta-analyses which use aggregated data. For these reasons, we decided to conduct a mega-analysis based on individual patient data (IPD) allowing to control for these variables and isolate the specific association between RCU and the severity of symptoms.

**Objectives:** Investigate the association between RCU on the positive, negative, general, and disorganized symptoms of psychosis as assessed by the Positive and Negative Syndrome Scale (PANSS), accounting for individual-level confounding variables.

**Methods:** IPD were requested by email to corresponding authors of published articles that measured RCU and PANSS scores in subjects with schizophrenia-spectrum disorders, based on a screening process on PubMed, ScienceDirect and PsycINFO databases. A two-stage random effect multivariate IPD meta-analysis was then performed, to isolate the direct association between RCU and the 'positive', 'negative', and 'general' dimensions of schizophrenia-spectrum disorders. Confounding variables were included in the models when available in the original dataset.

**Results:** 65 publications were eligible for inclusion. 18 authors agreed to provide their IPD. A total of 16 datasets were usable, regrouping 3,346 individual participant data, with 2,827 complete cases. Regression coefficients extracted after the first stage were adjusted for at least sex and age across all studies. RCU was found to be significantly associated with heightened positive symptoms severity (MD = 0.41, 95% CI [0.0; 0.82],  $p = 0.04$ ), whereas it appeared significantly associated with less severe negative symptoms (MD = -0.63, 95% CI [-1.1; -0.17],  $p = 0.008$ ). No significant association was found between RCU and general symptoms (MD = -0.24, 95% CI [-0.69; 0.21];  $p = 0.29$ ), as well as disorganization (MD = -0.08, 95% CI [-0.47; 0.35],  $p = 0.63$ ).

**Conclusions:** Our results allow for a general and subtle overview of the association of RCU with symptoms of psychosis. Our findings suggest a double and paradoxical effect of cannabis, which could both exacerbate positive symptoms and alleviate negative symptoms. This supports both the hypotheses of a disease aggravator and self-medication.

*Results change as we receive datasets from collaborating authors and could continue to change as not all authors sent their datasets yet.*

**Disclosure of Interest:** None Declared

## EPP1035

### Rituximab for treatment-resistant schizophrenia and/or obsessive-compulsive disorder (OCD): functional connectivity and cytokines associated with symptomatic improvements

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**Introduction:** Immunological mechanisms may contribute to the causation of mental illness. Autoimmunity is most convincingly

shown for anti-NMDA-R encephalitis and Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS); disorders that overlap clinically with schizophrenia and OCD. Altered inflammatory cytokine production, glial activation and auto-antibodies have also been associated with schizophrenia and OCD. In these disorders, however, the treatment results with anti-inflammatory or immunomodulating drugs have hitherto been limited and inconsistent. Yet other targets within the immune system may still be effective and new options are warranted for treatment-resistant patients. Rituximab targets B-lymphocytes and is often used in autoimmune disorders such as rheumatoid arthritis, multiple sclerosis and anti-NMDA-R encephalitis.

**Objectives:** We aimed to investigate whether rituximab is clinically effective, safe and tolerable as add-on therapy in markedly ill, treatment-resistant adult psychiatric patients with schizophrenia or OCD. We also wanted to identify putative mediating mechanisms in treatment responders, such as cytokine changes and functional connectivity (FC).

**Methods:** In an open pilot study, adults (18-39 years) with treatment-resistant schizophrenia and/or OCD were included. They received an intravenous infusion of rituximab 1000 mg, once at baseline, in addition to their regular psychiatric medication and were followed for 1 year. The main outcome measures were the Positive and Negative Syndrome Scale (PANSS) or Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the Clinical Global Impression-Improvement scale (CGI-I) and the Personal and Social Performance scale (PSP). Treatment response was defined as  $\geq 40\%$  decrease in PANSS or  $\geq 35\%$  decrease in Y-BOCS, and much improved according to CGI-I. Resting-state fMRI was applied at baseline and after 5 months. Plasma cytokines were measured at 0, 3 and 5 months. Cognitive tests and the recently developed PsychoNeuroinflammatory Related Signs and Symptoms Inventory (PNISSI) were used to identify and measure symptoms related to neuro-inflammation and cognitive function.

**Results:** Nineteen patients were treated with rituximab. 3-5 months after treatment, 6/9 patients with schizophrenia and 1/10 with OCD responded. One schizophrenia patient continues with rituximab every 6 months and has reportedly done well for almost 3 years. No severe side effects were reported apart from recurrent abdominal pain in a schizophrenia patient and one case of post-COVID-19 syndrome. Significant changes of FC were detected in responders only and correlated with PSP changes.

**Conclusions:** Aberrant B-cell activities may contribute to treatment-resistant schizophrenia and be amenable to treatment with rituximab. However, the results of this pilot study need confirmation in placebo-controlled trials.

**Disclosure of Interest:** None Declared

## EPP1036

### Genital Self-Mutilation in a Patient with Psychosis: A Case of Klingsor Syndrome

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