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Persistent negative symptoms are associated with worse outcome in both first-episode and chronic subjects with schizophrenia. The identification of these symptoms in recent-onset subjects is still controversial as retrospective data are often unavailable. The prospective assessment of persistence of negative symptoms might represent a valid alternative but the length of the persistence is still to be established. The present study investigated the prevalence of negative symptoms of moderate severity, unconfounded by depression and extrapyramidal symptoms at baseline in a large cohort of patients in the early stage of a schizophrenia-spectrum disorder, recruited to the OPTiMiSE trial. Persistent unconfounded negative symptoms were assessed at 4, 10 and 22 weeks of treatment. Symptomatic remission, attrition rate and psychosocial functioning was evaluated in subjects with short-term (4 weeks) persistent negative symptoms (PNS) and in those with negative symptoms that did not persist at follow-up and/or were confounded at baseline (N-PNS). Negative symptoms of moderate severity were observed in 59% of subjects at baseline and were associated to worse global functioning. PNS were observed in 7.9% of the cohort, unconfounded at both baseline and end of 4-week treatment. PNS subjects showed lower remission and higher attrition rates at the end of all treatment phases. Fifty-six percent of subjects completing phase 3 (clozapine treatment) had PNS, and 60% of them were non-remitters at the end of this phase. The presence of short-term PNS during the first phases of psychosis was associated with poor clinical outcome and resistance to antipsychotic treatment, including clozapine.

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**Keywords:** First-episode schizophrenia; Functional Outcome; Persistent negative symptoms

## S0126

## Negative symptoms assessment in early intervention settings: Implications for early identification and treatment

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Negative symptoms are a core feature of schizophrenia spectrum disorders associated with poor outcomes such as low remission rates and impairments in daily functioning and quality of life in early psychosis. The assessment of negative symptoms in early psychotic disorders is predominantly conducted by use of first-generation scales such as the PANSS and the SANS, along with the SIPS and CAARMS for the psychosis clinical high-risk (CHR) state. Following the progressed conceptualization of negative symptoms, it has, however, been recognized that these scales suffer important methodological limitations. This warrants a use of second-generation scales such as the Brief Negative Symptom Scale (BNSS) and the Clinical Assessment Interview for Negative Symptoms (CAINS) in early intervention settings in order to achieve a more accurate assessment of the negative symptom complex. Advancing the assessment of negative symptoms in early psychosis may also guide more targeted intervention approaches aimed at improving functional outcome. Albeit recognizing that negative symptoms constitute an important barrier to a good functional outcome in psychotic disorders, few studies have directly aimed at alleviating negative symptoms in early psychosis. Meta-analytical evidence does, however, exist on the efficacy of the combined treatment modalities incorporated in Early Intervention Services (e.g. intensive and assertive case management, family involvement etc.) in reducing negative symptoms in first-episode psychosis. Evidence on the effect of interventions for improving negative symptoms in the CHR state is lacking. Developing targeted, and possibly more individualized negative symptoms treatment approaches, constitute an essential future research area.

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## S0128

## The challenges in schizophrenia treatment in real-life: The uncomfortable truth

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Certain percentage of the first-episode schizophrenia patients presents with negative symptoms, which persists over the year and influence treatment outcomes (Galderisi et al. 2013). Treatment of negative symptoms has been a significant continuous clinical challenge. Majority of recently published guidelines recommend antipsychotic monotherapy as the standard of care, recommending antipsychotic combination therapy only after a failed trial with clozapine (George A. Keepers et al. 2020; Faden et al. 2020). However, real-life forces clinicians to look for possible combinations of medications early on, especially to tackle negative symptoms. The systematic review of global prescribing practices covering four decades found the pooled median rate of antipsychotic combination therapy approximately 20% (Gallego et al. 2012). One of the largest retrospective studies every conducted (n = 62,250) assessed rehospitalisation rates and the long-term use of antipsychotic polypharmacy in schizophrenia. Antipsychotic combination treatment was associated with an approximate 10% lower relative risk of psychiatric rehospitalisation compared with antipsychotic monotherapy (Tiihonen et al. 2019). Real-world effectiveness study of antipsychotic monotherapy vs. polypharmacy in schizophrenia from Eastern Europe is also supporting this approach (Katona, Czobor, and Bitter 2014). At the same time antipsychotic combination therapy can increase the total antipsychotic dose burden, frequency of adverse effects, potential drug-drug interactions and incur additional costs. In our recent naturalistic study in schizophrenia outpatients (n=120) with insufficient effectiveness of previous antipsychotics

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