Methods: In the 8-week, multicenter, Phase III, double-blind, placebo-controlled, inpatient study (NCT02109562), adults 18–55 years with acute schizophrenia were randomized to monthly injections of placebo (N=112), RBP-7000 90 mg (N=111) or RBP-7000 120 mg (114). Eligible participants were required to have a PANSS total score 50–120 (inclusive) at screening and a score of ≥4 on at least 2 of the following PANSS Positive subscale items: hallucinatory behavior, delusions, conceptual disorganization, suspiciousness/persecution. In a post hoc analysis of this ITT population, a mixed-effects model for repeated measures with no multiplicity adjustments, was used to examine observed changes in the scores of the 30 individual PANSS items from baseline at day 57.

Results: Compared with placebo, treatment with either 90 mg or 120 mg RBP-7000 improved 4 out of 7 PANSS Positive items: hallucinatory behavior (90 mg: 120 mg, P<0.001), conceptual disorganization (90 mg: 120 mg, P<0.01), delusions (90 mg: 120 mg, P<0.05), and suspiciousness/persecution (90 mg: 120 mg, P<0.05). Additionally, improvements in hostility (P<0.01) and excitement scores were observed with RBP-7000 120 mg vs placebo (P<0.01).

Treatment with RBP-7000 120 mg also improved 2 PANSS Negative item scores (emotional withdrawal [P<0.01] and passive/athetoid withdrawal [P<0.05]), while stereotyped thinking (P=0.054) and difficulty in abstract thinking (P=0.07) trended toward improvement.

Both RBP-7000 doses improved 6 of 16 PANSS General Psychopathology item scores vs placebo: depression (90 mg: 120 mg, P<0.001), active social avoidance (90 mg: 120 mg, P<0.05), poor attention (90 mg: 120 mg, P<0.05), anxiety (90 mg: 120 mg, P<0.05), and tension (90 mg: 120 mg, P<0.05). Improvements in poor impulse control (P<0.001) and somatic concern (P<0.05) were also observed with RBP-7000 120 mg, while the 90 mg dose improved motor retardation (P<0.01).

Discussion: Treatment with both 90 mg and 120 mg of RBP-7000 improved the majority of PANSS items. Importantly, treatment with the higher 120 mg dose resulted in improvement on 2 PANSS Negative items, suggesting RBP-7000 may be useful in addressing difficult to treat negative symptoms.

F28. CLINICAL VALIDATION OF THE GLASGOW ANTIpsychotic SIDE EFFECT SCALE (GASS)

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Background: Antipsychotics are the mainstay in the treatment of schizophrenia and other psychotic disorders. Treatment with antipsychotics is associated with significant side effects, including weight gain, sedation and Parkinsonism. These side effects may reduce the quality of life and result in poor treatment adherence. Therefore, regular screening and monitoring of side effects is essential to ensure optimal treatment adjustment and outcomes. The UKU side effect scale (UKU) is the most comprehensive tool used to assess multi-domain side effects. This scale is administered by trained health care professionals based on a long semi-structured interview that precludes its widespread clinical use. In order to implement routine side effect screening and monitoring in real-world settings, a less time-consuming rating scale is needed. The Glasgow Antipsychotic Side Effect Scale (GASS) is a patient self-report scale developed exactly for this purpose. Until now, GASS has only been validated using other self-report side-effect rating scales as the reference, which is suboptimal from a validation perspective. Therefore, the aim of the present study was to perform a clinical validation of the GASS using the health care professional-administered UKU assessment as the gold standard reference.

Methods: Participants must be ≥18 years old, have a diagnosis of a psychotic disorder (ICD-10: F2x.x) and receive treatment with an antipsychotic at the outpatient clinic, Department for Psychiatry, Aarhus University Hospital, Denmark. Each participant will self-rate his/her side effects on the GASS. Additionally, the participants will fill in the 5-item World Health Organization well-being index (WHO-5). Subsequently, one of three trained raters will conduct the UKU interview and rate the participant’s side effects. The scores on the GASS items will be compared with the scores on the corresponding items on the UKU. The statistical analyses will include calculation of specificity, sensitivity, positive predicative value, and negative predictive value of the GASS as well as the intraclass correlation coefficient.

Results: Preliminary results of the study: Altogether 81 antipsychotic-treated outpatients with schizophrenia-spectrum disorders (age= 42.3±13.4 years, males=43.3%, schizophrenia=76.5%) completed the GASS and were subsequently rated on the UKU-SERS-Clin by a trained rater. Statistical analysis showed satisfactory values with sensitivity values >75%, specificity values >70% and NPV >79% for the majority of GASS items. Time to complete all items of the GASS (n = 57 with complete data) was 3.8 (±2) minutes. Further, the GASS total score was negatively correlated with the WHO-5 total score. The full results of the study will be presented at the SIRS 2019 conference.

Discussion: The GASS was shown to have acceptable properties for a self-rated side effect screening tool and can be implemented in clinical practice to aide measurement-based care and decision-making.

F29. EXPLORATORY ANALYSIS OF THE RELATIONSHIP BETWEEN THE CHANGE FROM BASELINE IN PANSS AND BNNS RATING SCALES

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Background: Schizophrenia with predominant negative symptoms represents a significant unmet medical need. New instruments measuring the severity of negative symptoms are being implemented into clinical trials to improve the ability to accurately measure these symptoms. We have previously reported on the relationship between the Positive and Negative Syndrome Scale and the Brief Negative Symptom scales. In the current analysis we intend to assess the relationship between the change from baseline in the BNSS scale and change from baseline in PANSS negative subscale and PANSS negative factor(NFS). Additionally, we explored the relationship in change in the avolition/apathy factor as well as the expressive deficits factor between the BNSS and the PANSS. Given the exploratory nature of the analyses we did not correct for multiplicity.

Methods: Data from 82 schizophrenia clinical trials subjects with both PANSS and BNSS data available were used. Controlling for baseline severity using the baseline CGI severity score we conducted exploratory regression analyses assessing the relationship between the change from baseline in the BNSS scale and change from baseline in PANSS negative subscale and PANSS negative factor(NFS). Strong correlations were identified in change from baseline between BNSS scale and the PANSS NFS and the PANSS negative subscale (r = 0.67 and r = 0.62, respectively). The following equations were derived:

\[ \Delta\text{BNSS} = 3.84 + 1.75 \times \Delta\text{PANSS-negative} - 1.31 \times \text{CGI-SBaseline} \]

\[ \Delta\text{BNSS} = 5.46 + 1.75 \times \text{PANSS-negative} - 1.31 \times \text{CGI-SBaseline} \]

Discussion: Our data indicate strong relationship between the change in BNSS total score and change in PANSS negative subscale / negative factor from baseline. In addition, our data indicate a considerably weaker
relationship between the changes from baseline in the apathy/avolition and expressive deficit factors between the BNSS and the PANSS. We hypothesise that the main reason for this decrease in correlation between the two instruments on the factor level is driven by the underlying differences in the construction of the respective scales. Unlike the PANSS, the BNSS addresses all five currently recognized domains of negative symptoms including anhedonia and attempts to differentiate anticipatory from summatory states. While on the total score level the BNSS and the PANSS negative subscale/negative factor capture change from baseline in a very similar fashion, the differences on the level of the apathy/avolition and expressive deficit factors offer the potential to assess the change from baseline in a more granular way and therefore justify the use of both instruments simultaneously during a clinical trial. We plan to replicate the results on larger datasets.

**F30. QUINTUPLE HYPOTHESES TARGETED IN SCHIZOPHRENIA: FIGHT FIRE WITH FIRE**

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**Background:** There are no effective treatments available or on the horizon for cognitive impairments associated with schizophrenia (CIAS) and primary negative symptoms. Cholinergic and glutamatergic systems, alpha-7 nicotinic acetylcholine receptor (alpha-7nAChR), and N-methyl-D-aspartate receptor (NMDA-R) have been implicated in the pathophysiology of CIAS and primary negative symptoms. Seven studies in animals showed that the galantamine-memantine combination was effective for cognition—synergistic benefits were also seen. The galantamine-memantine combination was significantly better for cognition than the donepezil-memantine combination in patients with Alzheimer’s disease. There is evidence that kynurenic pathway (KY) metabolites are associated with CIAS and deficit syndrome. Kynurenic acid (KYNA) is elevated in schizophrenia and is an antagonist of the alpha-7nAChR and NMDA-R. The aim of this study was to examine whether the galantamine-memantine combination is effective for CIAS.

**Methods:** In this 6-week open-label clinical trial, three participants with schizophrenia were enrolled; two completed the study. Participants received galantamine ER 24 mg and memantine XR 21 mg for four weeks. Plasma was analyzed for KP metabolites.

**Results:** In a 36-year-old man with schizophrenia, scores improved in five of seven MATRICS Consensus Cognitive Battery (MCCB) domains; the exceptions were working memory and verbal learning. Also, the Scale for the Assessment of Negative Symptoms total score decreased from five to zero. This finding is suggestive of primary negative symptoms because the Brief Psychiatric Rating Scale, Simpson Angus Scale, and Calgary Depression Scale for Schizophrenia scores were minimal, and the urinary drug screen was negative at baseline and endpoint. In a 45-year-old man with schizophrenia disorder, there were improvements in speed of processing and working memory. Picolinic acid (PIC) concentration decreased in both participants. KYNA concentration decreased in both participants, and kynurenine concentration decreased in one participant.

**Discussion:** This is the first study that is suggestive of the association of MCCB and KP metabolites in schizophrenia. The decrease in PIC concentration with the treatment is a promising finding because high concentrations of PIC are toxic to the brain. Although this pilot study is not powered, the data are promising. RCTs are warranted to validate the findings. “Repurposing” of approved medications such as galantamine and memantine could lead to rapid clinical implementation if the results of RCTs are positive. This study is the first in which the nicotinic-cholinergic and glutamatergic systems were simultaneously targeted in people with schizophrenia. In addition, the galantamine-memantine combination (unique and novel) has synergistic effects of alpha-7nAChR and NMDA-R. The galantamine-memantine combination targeting both receptors concurrently is a paradigm shift in schizophrenia because until now only one receptor (NMDA or nicotinic with partial treatment response) has been targeted at a time. This combination may broaden the number of cognitive domains that may significantly improve compared to placebo and potentially increase the composite score. The pathophysiological mechanism of mismatch negativity may occur via interactive effects of alpha-7nACh and NMDA receptors. This combination targets the quintuple hypotheses (dopamine, nicotinic-cholinergic, glutamatergic/NMDA, GABA, and KYNA) concurrently and has the potential to treat positive, cognitive, and primary negative symptoms. The galantamine-memantine combination has the potential to become the first anti-schizophrenia treatment.

**F31. WHAT ARE THE IMPLICATIONS OF RECRUITMENT SOURCE (CLINICAL OR NON-CLINICAL) IN SCHIZOPHRENIA TRIALS FOR SUCCESSFUL RECRUITMENT AND RETENTION IN TERMS OF SCREEN FAILURE, OR NON COMPLETION OF TRIAL?**

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**Background:** Recruitment is one of the greatest challenges in performing randomized controlled trials. The recruitment environment is a competitive one, with a large number of studies recruiting from a finite patient pool. Commercial pressures mean products are moved through the research and regulatory process as quickly as possible. This often results in ambitious recruitment targets. As a result, recruitment strategies often move beyond the traditional, clinically-driven approaches that focus on a Principal Investigator’s (PI) own patient list and that of their wider clinical network, and towards strategies such as online recruitment, community outreach approaches, self-referral and other approaches (hereafter termed collectively as ‘Non-Clinical’ approaches).

Whilst these approaches bring more potential participants to a study, it has not been established what implications there are for quality of participant in terms of recruitment and retention. This poster examines whether research participants from Clinical (C) and Non-Clinical (NC) sources differ in two aspects—levels of study randomization and of study completion.

**Methods:** Recruitment source data were gathered from four Phase 3 and one Phase 4 clinical trials in schizophrenia. 3258 patients were classified as either C referrals (i.e. PI’s own patient, referral from another practitioner, or research database) or NC referrals (from advertising, internet-derived referrals, self-referrals, or outreach programs). Chi-square analyses were carried out to examine goodness-of-fit.

**Results:** For combined data from all trials, highly significant differences were found between C and NC referrals for number of patients randomized vs number not randomized (p <.001). C referrals were highly significantly more likely to randomize (also significant for each study individually). Highly significant differences were also found for patients who randomized, but completed the study vs those who randomized, yet failed to complete the study (p <.01) also significant for four out of five studies individually. Patients from C referral sources who randomized, yet failed to complete the study (p <.01) also significant for four out of five studies individually. Highly significant differences were also found for patients who randomized, but completed the study vs those who randomized, yet failed to complete the study (p <.01) also significant for four out of five studies individually. Highly significant differences were also found for patients who randomized, but completed the study vs those who randomized, yet failed to complete the study (p <.01) also significant for four out of five studies individually.

**Discussion:** Whilst the division between C and NC sources of data is arbitrary, it does possess face validity. In addition, these data would suggest that it possesses some clinical validity. The significantly different rates of study randomization and completion indicate underlying qualitative differences between these sources of referrals. A number of factors might be hypothesized to underlie these differences, amongst them implicit pre-screening by...