**T26. CLINICAL OUTCOME ASSESSMENTS FOR TRIALS IN COGNITIVE IMPAIRMENT ASSOCIATED WITH SCHIZOPHRENIA**

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1Cogstate

**Background:** For clinical development programs in cognitive impairment associated with schizophrenia (CIAS), it has been stated that significant improvement on a cognitive performance endpoint would be necessary, but not sufficient, for drug approval. In addition, regulators require improvement on a functionally meaningful co-primary. A co-primary approach may require a more conservative criterion to be set for statistical significance: first a modest impact of correlation between the endpoints is observed on required sample size for a given effect size and power; second a more important impact of effect size is observed. If the standardized effect size for one endpoint is smaller, the sample size is determined by this. In the recent draft guidance for treatment of early AD, the FDA acknowledge the entity of cognition as meaningful and they outline circumstances in which integrated cognition-function, or cognition only outcomes would be acceptable as single primary endpoints. In addition, it is stated that when measured using conventional assessments, the meaningfulness of cognition may not be apparent.

**Methods:** A review was conducted of Phase 2 and 3 industry clinical trials for schizophrenia listed on clinicaltrials.gov, and which studied potential for cognitive improvement. Fifty-two trials were identified and the most commonly reported outcomes for cognition and function identified.

**Results:** The most commonly used and reported outcomes have been the MCCB for cognition and the UPSA for function. The other cognitive outcomes used most frequently (≥7 trials) have been the Cogstate, and BACS batteries, whilst the other most frequently used functional outcomes (≥5 trials) have been the SCOR and PSP. Furthermore, several versions of the UPSA have been employed (e.g. UPSA-B, UPA-2, UPSA-VIM). These clinical outcome assessments (COAs) fall into groups of cognitive performance-based outcome (PerfO), functional capacity assessments, and clinician-reported outcome (ClinRO) assessments. Whilst no treatment is approved for CIAS, several trials have shown encouraging data in early clinical development and certain antipsychotic trials have also shown evidence for improvement.

**Discussion:** Cognition as measured by conventional cognitive PerfO assessments is most commonly an indirect measure of meaningful health outcomes (i.e. the test activities are not a part of a person’s usual normal life). Consequently, the meaning of any change in a cognitive score is not intrinsically known. This lack of direct measurement of meaningful health outcomes drives the requirement for the use of co-primary endpoints. There may be alternate approaches such as establishing cognitive only outcomes as intermediate or surrogate endpoints or creating integrated cognition-function endpoints with greater statistical power. Sufficient data likely exist across completed industry trials to facilitate the development and validation of such endpoints. Furthermore, novel cognitive PerfO may be developed that are more direct measures of health outcomes and could also form single primary endpoints.

**T27. DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH DURATION OF UNTREATED PSYCHOSIS (DUP) IN ANTIPSYCHOTIC NAIVE FIRST EPISODE PSYCHOSIS (FEP)**

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**Background:** Depressive symptoms are common on first episode psychosis, with a prevalence of up to 83% of a full depressive episode. These symptoms are related to worst functionality and higher suicide rates. In literature, longer duration of untreated psychosis (DUP) and a worse premorbid are related to these symptoms. DUP is one of the most modifiable factors on FEP, with shorter DUP predicting better outcomes in patients with schizophrenia. Only a few studies explore the relation between depressive symptoms and DUP, with no studies in a Brazilian population. Therefore, our aim was to investigate the association between depressive symptoms, functionality and DUP of antipsychotic naive-FEP (AN-FEP) patients in a 10-week follow-up study.

**Methods:** We recruited 88 AN-FEP patients with first episode psychosis admitted to a psychiatric emergency service. We assessed diagnosis according to Structured Clinical Interview for DSM-IV (SCID-I). Depressive symptoms were measured with the depressive dimension of Positive and Negative Symptoms Scale (PANSS), the Calgary Depression Scale for Schizophrenia (CDSS) and the Clinical Global Impression Scale (CGI-S). We adopted the CDSS cut-off of 6, according to the Brazilian validation. All patients were treated with risperidone and evaluated after 10 weeks. For analysis, we performed non-parametric correlation tests (Spearman’s correlation).

**Results:** Prevalence of depressive syndrome according to CDSS was 20.4% at baseline, and 11.1% after treatment. Also, 4.6% of the patients started an antidepressant treatment. We found a mean DUP of 166 days (SD = 282, median = 47 days). We found a correlation between DUP and depressive dimension at baseline (r = -0.397; p < 0.001) and on follow-up (r = -0.322, p = 0.012). At both assessments, CDSS and the depressive scale of CGI-S had a correlation.

**Discussion:** Prevalence of depression and median DUP was in line with the worldwide range. Surprisingly, this is the first study that shows a negative correlation between depressive symptoms and DUP, which is opposite to what most studies demonstrates and to what we expected. Depression is a common feature in FEP, yet their risk factors remain unclear. The relation between DUP and depressive symptoms should be more studied to understand the real influence of DUP in these patients.

**T28. A COMPARISON BETWEEN OLanzAPINE CONTINuation AND AMIsULPride COMBINATION IN ACUTE SCHIZOPHRENIA PATIENTS SHOWING EARLY NON-RESPONSE TO OLanzAPINE: 4-WEEKS, RANDOMIZED, RATER-BLINDED PILOT STUDY**

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**Background:** As we know, olanzapine is the most commonly prescribed antipsychotic medication and it was the first approved atypical antipsychotic. A major disadvantage of olanzapine is its weight gain, which often results in patients discontinuing treatment within weeks of initiation. This study compared olanzapine continuation with amisulpride combination in acute schizophrenia patients showing early non-response to olanzapine.

**Methods:** Patients were randomized to olanzapine continuation (7.5 mg/day) or olanzapine/amisulpride combination (olanzapine 15 mg/day, amisulpride 600 mg/day) for 4 weeks. The primary outcome measure was the change in weight from baseline to final visit.

**Results:** A total of 20 patients were enrolled in the study. The baseline characteristics were well balanced between the two groups. The mean change in weight from baseline to final visit was -1.6 kg in the olanzapine group and -3.2 kg in the olanzapine/amisulpride group (p = 0.04). The difference in weight change between the two groups was significant.

**Discussion:** This study suggests that olanzapine/amisulpride combination is a promising treatment option for acute schizophrenia patients showing early non-response to olanzapine. Further research is needed to confirm the findings in larger studies.