F44. AN ADD-ON TRIAL WITH N-ACETYL-CYSTEINE (NAC) IN EARLY PSYCHOSIS PATIENTS: TOWARDS BIOMARKER GUIDED TREATMENT

Methods: Here, we report preliminary data on the possible efficacy of tiagabine (Gabitril), which is a selective uptake inhibitor of the GABA (gamma-aminobutyric acid) transporter GAT-1, in the treatment of recent-onset schizophrenia. Subjects were randomized to receive either tiagabine or placebo added on to their antipsychotic regimen.
Results: Our data suggest that treatment with tiagabine during the early course of the illness can modulate PFC activation, as demonstrated by functional magnetic resonance imaging during working memory, and improve negative symptoms.
Discussion: Taken together, the proposed treatment strategy represents an effort to actively translate preclinical findings in SZ research into clinically testable hypotheses. This kind of translational approach, we believe, will ultimately lead to breakthrough in the treatment and possible prevention of SZ.

F44. AN ADD-ON TRIAL WITH N-ACETYL-CYSTEINE (NAC) IN EARLY PSYCHOSIS PATIENTS: TOWARDS BIOMARKER GUIDED TREATMENT

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Background: Oxidative stress, coupled with dysregulation of inflammation, NMDAR and dopamine, is involved in schizophrenia (SZ) pathophysiology. Earlier add-on clinical trials showed in chronic SZ patients that NAC, a precursor of glutathione (GSH), an important cerebral antioxidant, improved negative symptoms, mismatch negativity and local synchronization. We hypothesized that NAC at an earlier stage of illness would have a greater impact.
Methods: Early psychosis patients (EP, less than 5 years of illness, N=63; NAC=32, placebo=31) were supplemented with NAC (2.7g/day, 6 months) in a double-blind randomized placebo-controlled trial. Outcome measures: PANSS and neurocognition (MATRICS Consensus Cognitive Battery; n=36); quantification of medial prefronfal cortex glutathione (GSHmPFC) by 1H-magnetic-resonance-spectroscopy, of white matter diffusion properties estimated by generalized fractional anisotropy (gFA) computed from diffusion spectrum imaging (DSI), of blood cells GSH (GSHBC) and GSH peroxidase activity (GPxBC) at start and end of trial
Results: While PANSS negative and positive were not affected by NAC, NAC improved Processing Speed (NAC > Placebo; $F(1, 30)=5.849$, $p=.022$), favoring 2 of 3 processing speed tasks (Trail Making A, $F(1, 30)=4.279$, $p=.048$ & Verbal Fluency, $F(1, 30)=5.749$, $p=.023$). GSHmPFC (+23%, $p=0.005$) and GSHBC (+19%, $p=0.05$) were increased following NAC treatment. In patients with high-baseline GPxBC (>22.3U/gHb), subgroup explorations revealed an improvement of PANSS positive compared to placebo ($p=0.02$). The change of PANSS positive correlated negatively with that of GPxBC activity, showing that the improvement paralleled the restoration of redox status. NAC group showed 11% increase in fornix white matter integrity as measured by gFA, correlating with an increase in GSHmPFC over the 6-months period.
Discussion: This is the first clinical trial assessing the impact of NAC treatment in a sample of EP and the potential predictive role of peripheral biomarkers of redox dysregulation. The hypothesis that NAC would be beneficial to negative symptoms in EP was not confirmed in this small sample, most likely in reason of their very low level at baseline. The NAC induced GSHmPFC increase demonstrates its target engagement. NAC improved Processing Speed showing a therapeutic enhancement of cognitive functions. Most importantly, NAC improved fornix integrity, in association with brain GSH elevation, demonstrating for the first time that a redox regulator can enhance structural connectivity. Peripheral redox status allows identifying a subgroup of patients with improved positive symptoms. Future biomarker guided antioxidant interventions in larger EP samples should replicate these findings.

F45. THE EFFICACY AND SAFETY OF BLONASERIN AFTER SWITCHING FROM OTHER ATYPICAL ANTIPSYCHOTICS IN SCHIZOPHRENIC INPATIENTS: AN OPEN-LABEL, MULTI-CENTER TRIAL

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Background: The aim of this study was to investigate the efficacy and safety of blonanserin treatment after switching from other atypical antipsychotics in schizophrenic inpatients who showed inadequate efficacy and poor tolerability.
Methods: A total of 63 schizophrenic inpatients (inadequate response group=45 and poor tolerability group=18) were included in this study. They were already treated with atypical antipsychotics except blonanserin and not favored due to inadequate responses or intolerable adverse effects. Blonanserin was administered during 12 weeks after switching from their previous antispsychotics. Treatment response was evaluated with Brief Psychiatric Rating Scale (BPRS) and CGI-S, and safety profile were measured with Abnormal Involuntary Movement Scale (AIMS), Simpson-Angus Extrapyramidal Side effects Scale (SAR)S and Barnes Akathisia Rating Scale (BARS). Drug Attitude Inventory (DAI-10) and Subjective Well-being Under Neuroleptic Treatment (SWN) were used for subjective estimates. Assessments were done at baseline, 1, 2, 4, 8 and 12 weeks after blonanserin treatment. Repeated measures of ANOVA were done to analyze the group (inadequate vs. intolerable group) and time effects.
Results: CGI and BPRS were showed significant treatment responses after switching to Blonaserin. Time effects were significant at 2, 4, 8, 12 weeks after switching and group by time effect were also significant at that time. Mean changes of AIMS, SARS and BARS scores were not significant throughout test trial. Although SWN was significantly improved after switching to Blonaserin, it was not found significant group by time effect.
Discussion: The results suggest that blonanserin may be effective and well tolerable in schizophrenic patients who showed inadequate treatment response or poor tolerability.

F46. LUMATEPERONE (ITI-007): FAVORABLE SAFETY PROFILE IN AN OPEN LABEL SAFETY SWITCHING STUDY FROM STANDARD-OF-CARE ANTIPSYCHOTIC THERAPY IN PATIENTS WITH SCHIZOPHRENIA

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