T50. SYMPTOMATIC AND FUNCTIONAL RESPONSE TO BREXPIP RAZOLE TREATMENT IN PATIENTS WITH ACUTE SCHIZOPHRENIA BY AGE

Catherine Weiss*, Erin MacKenzie, Francois Therrien, Peter Zhang, Stine Meehan
1Otsuka Pharmaceutical Development & Commercialization, Inc; 2Lundbeck Canada, Inc; 4H. Lundbeck AIS

Background: Atypical antipsychotics are the mainstay of treatment for schizophrenia, and have a meaningful effect on positive symptoms and agitation/aggression. More recently, treatment goals have shifted to target functioning: a cycle of deterioration often occurs in early schizophrenia in which recurring relapse results in decreased functioning.

Brexipiprazole is a serotonin-dopamine activity modulator that is a partial agonist at 5-HT1A and dopamine D2 receptors, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors, all at subnanomolar potency. The efficacy of brexipiprazole has been shown in both short- and long-term studies. In this post-hoc analysis from three short-term studies, the proportion of patients achieving symptomatic and functional response was assessed, grouped by age at baseline.

Methods: Efficacy and functioning data were pooled from three 6-week, double-blind, placebo-controlled studies in hospitalized patients with acute exacerbation of schizophrenia (Vector [NCT01396421]; Beacon [NCT01396613]; and Lighthouse [NCT01810380]), and stratified according to age at baseline (18–35 years; and 36–65 years). For the current analyses, response was defined as reduction in PANSS score of ≥30% from baseline; a CGI-I score of 1 or 2 (much improved or 2). Functional response was defined as an increase in PSP total score of at least 10 points. The analyses were conducted using a mixed-model repeated measures (MMRM) approach with all brexipiprazole doses pooled (2-4mg/day).

Results: 557 patients aged 18–35 years and 857 patients aged 36–65 years were analysed. For patients aged 18–35 years, a statistically significantly greater proportion of brexipiprazole-treated vs placebo-treated patients had symptomatic response after 6 weeks of treatment (PANSS ≥30%: 40.5% vs 28.7%, p<0.01; CGI-I 1 or 2: 39.9% vs 25.4%, p<0.001; PANSS ≥30% OR CGI-I score of 1 or 2: 46.2% vs 32.3%, p<0.01). Similar results were observed for patients aged 36–65 years (PANSS ≥30%: 48.7% vs 37.6%, p<0.01; CGI-I 1 or 2: 47.1% vs 37.2%, p<0.001; PANSS ≥30% OR CGI-I score of 1 or 2: 54.8% vs 41.6%, p<0.001). For patients aged 18–35 years, a statistically significantly greater proportion of brexipiprazole-treated vs placebo-treated patients had functional response after 6 weeks of treatment (PSP 10 points change: 46.3% vs 33.0%, p<0.01); similar results were observed for patients aged 36–65 years (49.2% vs 38.2%, p=0.01).

Discussion: The results of these analyses confirm that 6 weeks of treatment with brexipiprazole results in symptomatic and functional response in acutely ill schizophrenia patients in both younger patients (age 18 to 35 years) as well as older patients (age 36–65).

T51. TREATMENT OF NEGATIVE SYMPTOMS OF SCHIZOPHRENIA WITH TRANSCRANIAL CURRENT STIMULATION (TDCS): RESULTS OF RANDOMIZED, DOUBLE-BLINDED, SHAM-CONTROLLED TRIAL

Leandro Valiengo*, Pedro Gordon, Mauricio Serpa, Acioy Lacerda, Wagnér Gattaz, Martinus Van de Bilt, Helio Helkis, Andre Brunoni
1University of Sao Paulo; 2Centro de Pesquisa e Ensaios Clinicos Sinapse-Bairral

Background: The negative symptoms of schizophrenia cause significant distress and impairment. The treatment of them is a challenge, with medications having none or little effect. So, new treatments are necessary for this condition. The aim of the study was to ascertain the efficacy of tDCS in treating negative symptoms of schizophrenia.

Methods: This study was designed to be a randomized, sham-controlled, double-blinded trial using tDCS for the treatment of negative symptoms of schizophrenia. One-hundred (here we analyzed only 70% of the sample, the remaining will be presented at the meeting) patients will be enrolled and submitted to ten tDCS session over the left dorsolateral prefrontal cortex (anodal stimulation) and left temporo-parietal junction-left (cathodal stimulation), over 5 consecutive days, with 2 mA of current. Participants were assessed with clinical and neuropsychological tests before and after the intervention. The primary outcome was change (over time and across groups) in the scores of the Negative Subscale of Positive and Negative Symptoms Syndrome (PANSS). Our secondary outcomes consist of others scales as SANS (Scale of Assessment of Negative Symptoms), Calgary and the AHRIS (Auditory Hallucinations Rating Scale).

Results: From 70% of the sample the active tDCS was significantly superior to sham at endpoint at 6 weeks by negative sub scale of PANSS (mean difference, 3.5 points; SD=6.2; P<0.05). The total PANSS and the hallucinations scale had no differences between both groups. The other times of analysis were not found differences between sham and active groups. The others scales (Calgary and SANS) have not been evaluated yet.

Discussion: The results of our studies suggests a potential role of tDCS for the treatment of negative symptoms of schizophrenia. The effect size was small. This is the biggest study with tDCS for treating negative symptoms of schizophrenia until now. At the meeting all the data will be analyzed (100 patients), it these could change our preliminary results.

T52. N-ACETYL-CYSTEINE ADD-ON TREATMENT LEADS TO AN IMPROVEMENT OF FORNIX WHITE MATTER INTEGRITY IN EARLY PSYCHOSIS

Paul Klauser, Lijing Xin, Margot Fournier, Alessandra Griffa, Martine Cleuxis, Raoul Jenni, Michel Cuendol, Rolf Gruetter, Patric Hagmann, Philippe Conus, Philipp Baumann, Kim Q. Do
1Lausanne University Hospital; 2DP-CHUV (TIPP)

Background: Beneficial effects of N-acetyl-cysteine (NAC) on negative symptoms in chronic schizophrenia have been reported in two studies. A recent study in early psychosis from our group, did not report significant improvement in negative symptoms (potentially linked to the modest baseline levels) but showed improvement in cognition (i.e. processing speed) and an increase in the brain antioxidant glutathione (GSH) levels, indicating good target engagement. Indeed, research in animal models highlights the critical role of redox regulation by brain GSH for white matter maturation and maintenance. Given the strong evidence of white matter (WM) alterations in schizophrenia...