

Media Release: European College of Neuropsychopharmacology (ECNP)

“For the science and treatment of disorders of the brain”

[Clinical trial shows first treatment for ‘emotional flatness’ associated with schizophrenia](#)

Embargo until: 00.05 Central European Summer Time (Amsterdam), Monday 31 Aug 2015

Results of a clinical trial seem to show the first effective treatment for the negative symptoms – withdrawal, lack of emotion, and apathy – associated with schizophrenia. This work is presented at the European College of Neuropsychopharmacology conference in Amsterdam.

Schizophrenia is one of the most common serious mental health conditions, with around 1 in 100 people experiencing schizophrenia in their lifetime*. The main symptoms fall into 3 categories: positive symptoms, such as delusions and hallucinations; negative symptoms, such as lack of drive and social withdrawal; and cognitive symptoms, such as problems with attention and memory. The negative symptoms tend to persist, and don’t respond well to current treatment. Effective medicines (antipsychotics) exist for positive symptoms, but negative symptoms and cognitive impairment do not respond well to the available treatments.

Now the results of a new Phase III clinical trial indicate that the negative symptoms may be treatable with a new investigational drug, cariprazine, which binds to the D2 and D3 dopamine receptor with D3 preference. The researchers, all from the Gedeon Richter pharmaceutical company which developed the drug, enrolled 461 men and women in a randomised, double-blind clinical trial, to compare cariprazine against risperidone (which is commonly used to treat schizophrenia). Patients were treated for 26 weeks, with 77.4% of enrolled patients completing the trial. Full details of the trial are given in the abstract.

The outcomes were measured using a special subscale** of the PANSS scale (Positive and Negative Syndrome Scale) which is a standard method used for measuring symptom severity of patients with schizophrenia. After 26 weeks of treatment, it was found that cariprazine treatment group showed a statistically significant improvement in the PANSS-NFS scale relative to risperidone (-1.47; p=0.002). In addition to the effect on predominant negative symptoms of schizophrenia, patients who took cariprazine also performed significantly better on personal and social functioning than those who took risperidone. Full details of the trial are given in the abstract.

According to lead researcher Dr György Németh (Chief Medical Officer, Gedeon Richter):

“The positive symptoms of schizophrenia can be controlled by drugs, but this is the first study ever to show a significant effect of a compound on negative symptom compared to

another antipsychotic. It seems that with cariprazine, we may be able to treat both the positive and negative symptoms with a single medication.”

Commenting, ECNP Executive Committee Member Professor Andreas Meyer-Lindenberg said:

“Treatments for the negative symptoms of schizophrenia are still urgently needed as these are critical predictors for patient’s recovery and reintegration. The current results suggest that D3-dopaminergic mechanisms may play a role in both causing and treating emotional flatness, which deserve further confirmation”.

The trial was organised and supported by the Gedeon Richter pharmaceutical company, which developed cariprazine. The researchers report that the most frequent adverse events (incidence $\geq 5\%$) across both treatments groups were insomnia, headache, akathisia, worsening of schizophrenia symptoms, anxiety and somnolence. As this drug has not yet completed the approval process, no indication of the costs of the treatment is available.

The ECNP receives no sponsorship from Gedeon Richter Plc we are reporting this as work presented at the ECNP annual conference.

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Notes for editors

Please mention the European College of Neuropsychopharmacology conference in any story from this press release.

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Background

*<http://www.nhs.uk/conditions/Schizophrenia/Pages/Introduction.aspx>

** Negative Factor Scale of PANSS, PANSS-NFS

The ECNP

The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe.

ECNP organises a wide range of scientific and educational activities, programmes and events across Europe, promoting the exchange of high-quality experimental and clinical research and fostering young scientists and clinicians.

The 28th ECNP Congress takes place in Amsterdam from 29 August-1 September. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting between 5,000 and 7,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world.

Website: www.ecnp.eu

Abstract P.3.d.053 Cariprazine as monotherapy for the treatment of schizophrenia patients with predominant negative symptoms: a double-blind, active controlled trial M. DeBelle, G. Németh, E. Szalai, B. Szatmári, J. Harsányi, A. Barabácssy, I. Laszlovszky; *Gedeon Richter Plc., Medical Division, Budapest, Hungary*

Introduction: Cariprazine, a dopamine D3/D2 receptor partial agonist with preference for D3 receptors, has demonstrated efficacy for the treatment of schizophrenia, including in three 6-week, randomized, double-blind, placebo-controlled, phase II/III clinical trials in patients with acute psychotic exacerbations and in one relapse prevention clinical trial in stabilized patients. Post hoc analysis of the 6-week efficacy trials on a subset of patients with high levels of negative symptoms demonstrated significantly greater improvement relative to placebo [1, 2]. The objective of this clinical trial was to evaluate the efficacy, safety, and tolerability of cariprazine relative to another antipsychotic in an adequate and well-conducted clinical trial in patients with predominant negative symptoms of schizophrenia.

Methods: This study was a multinational, randomized, double-blind, risperidone-controlled, parallel group clinical trial in adult patients with predominant, negative symptoms of schizophrenia. To be enrolled in the clinical trial and randomized to study treatment, patients had to have with predominant negative symptoms, defined as PANSS factor score for negative symptoms (PANSS-FSNS) ≥ 24 and at least 2 of the 3 core negative symptoms scored at least 4; PANSS factor score for positive symptoms (PANSS-FSPS) ≥ 19 ; no clinically relevant depressive symptoms and no or limited extrapyramidal symptoms; assessed as stabilized with predominant negative symptoms for a retrospective 6-month period prior to screening, and for a prospective 4-week period prior to randomization. Following 2 weeks of cross-titration and discontinuation of previously taken antipsychotic(s), patients were treated with either cariprazine target dose 4.5 mg/d, or with risperidone target dose 4 mg/d for 24 weeks. The primary efficacy parameter was the improvement in negative symptoms, defined as change from baseline (CfB) to endpoint in PANSS-FSNS. The secondary efficacy parameter was functional improvement, defined as CfB to endpoint in Personal and Social Performance Scale (PSP) total score.

Results: 461 patients were randomized 1:1 to double-blind risperidone (n = 231) or cariprazine (n = 230) treatment. PANSS-FSNS (27.5 in risperidone, 27.7 in cariprazine treatment groups, respectively), PSP total score (48.1, 48.8 respectively) and PANSS-FSPS (8.6, 8.8 respectively) were similar at baseline in the two treatment groups. 77.4% of the patients completed the 26-week study treatment duration, in both groups. CfB at week 26 in the primary parameter, PANSS-FSNS, was significantly larger in the cariprazine treatment group than in the risperidone treatment group (LSMD = -1.47; 95% CI: [-2.39, -0.53]; p = 0.002; MMRM, ITT). CfB at week 26 in the secondary parameter, PSP total score, showed similarly a significantly greater improvement with cariprazine when compared to risperidone (LSMD = 4.63; 95% CI: [2.71, 6.56]; p < 0.001; MMRM, ITT). Patients tolerated the study treatment well, as reflected by low discontinuation rates due to AEs. The most common adverse events ($\geq 10\%$) during study treatment were insomnia (10.0%), and headache (10.4%), both in the risperidone treatment group.

Conclusions: 26-week cariprazine treatment, given as antipsychotic monotherapy, was significantly more effective on negative symptoms and on functioning than risperidone in patients with predominant negative symptoms of schizophrenia. Cariprazine treatment was generally well tolerated in this study.

References [1] Debelle, M., Faradzs-zade, S., Szatmari, B. et al., 2014. Cariprazine in negative symptoms of schizophrenia: Post hoc analyses of a fixed-dose, placebo and active controlled trial. *Eur Neuropsychopharm* 24 (Suppl. 1), S534. [2] Debelle, M., Faradzs-zade, S., Szatmari, B. et al., 2015. Cariprazine in negative symptoms of schizophrenia: Post hoc analyses of a fixed-dose Phase III, randomized, double-blind, placebo- and active-controlled trial, EPA15-0567, Abstract 0242, Vienna.

Disclosure statement: The study was supported by Gedeon Richter Plc.