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Efficacy of Cariprazine in Predominant Negative Symptoms of Schizophrenia – Post Hoc Analyses Against Different Comparators

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INTRODUCTION

- Long-term treatment with antipsychotic agents is indicated for all patients with schizophrenia.
- Treatment of predominant negative symptoms (PNS) with available antipsychotics may lead to worsening of the targeted symptoms as they are associated with unpleasant adverse effects which mimic negative symptoms including extrapyramidal symptoms (EPS), dysphoria, depression, sedation, etc. (Benkert, 2014)
- Choosing the right agent to treat negative symptoms can therefore be challenging. With no effective therapies available for PNS, various treatment approaches are applied (even taking patients off medication), although these options are suboptimal.
- Cariprazine, a potent dopamine D3/D2 receptor partial agonist with preferential binding to D3 receptors, is approved in the EU for the treatment of schizophrenia in adults and in the US for the treatment of schizophrenia and manic or mixed episodes associated with bipolar I disorder.
- Cariprazine has been shown to be effective in the treatment of PNS in a large scale, double-blind, active-controlled clinical trial (Németh, 2017)

STUDY OBJECTIVE

The objective of this poster is to present efficacy data of cariprazine versus different comparators (risperidone, aripiprazole, placebo) in the treatment of PNS.

METHODS

Study Design

- Data of PNS patients were analyzed from 3 different clinical studies:
  - **Study-1** A randomized, double-blind, risperidone-controlled 26-week study in the specific subpopulation of PNS patients (Németh, 2017);
  - **Study-2** A randomized, double-blind, placebo and aripiprazole controlled 6-week study in patients with acute schizophrenia (Durgam, 2015);
  - **Study-3** A randomized, double-blind, placebo-controlled, relapse prevention study investigating cariprazine versus placebo in the long-term maintenance treatment (Durgam, 2016).
- PNS patients were defined as having a score of ≥ 24 on the Positive and Negative Syndrome Scale Factors Score for Negative Symptoms (PANSS-FSNS ≥ 24) and of ≤ 19 on the PANSS Factors Score for Positive Symptoms (PANSS-FSPS ≤ 19). For Study-1 patients were enrolled into the study based on the above inclusion criteria. For Study-2 and Study-3 the above inclusion criteria were used for the post hoc analyses.
- For the efficacy analyses change from baseline to end on the PANSS-FSNS was analyzed.
- Patients receiving cariprazine were grouped into pooled dose groups. Only patients receiving a modal daily dose within the EMA/FDA approved dose range (1.5-6 mg) for each patient population were included in the analyses

Data analyses

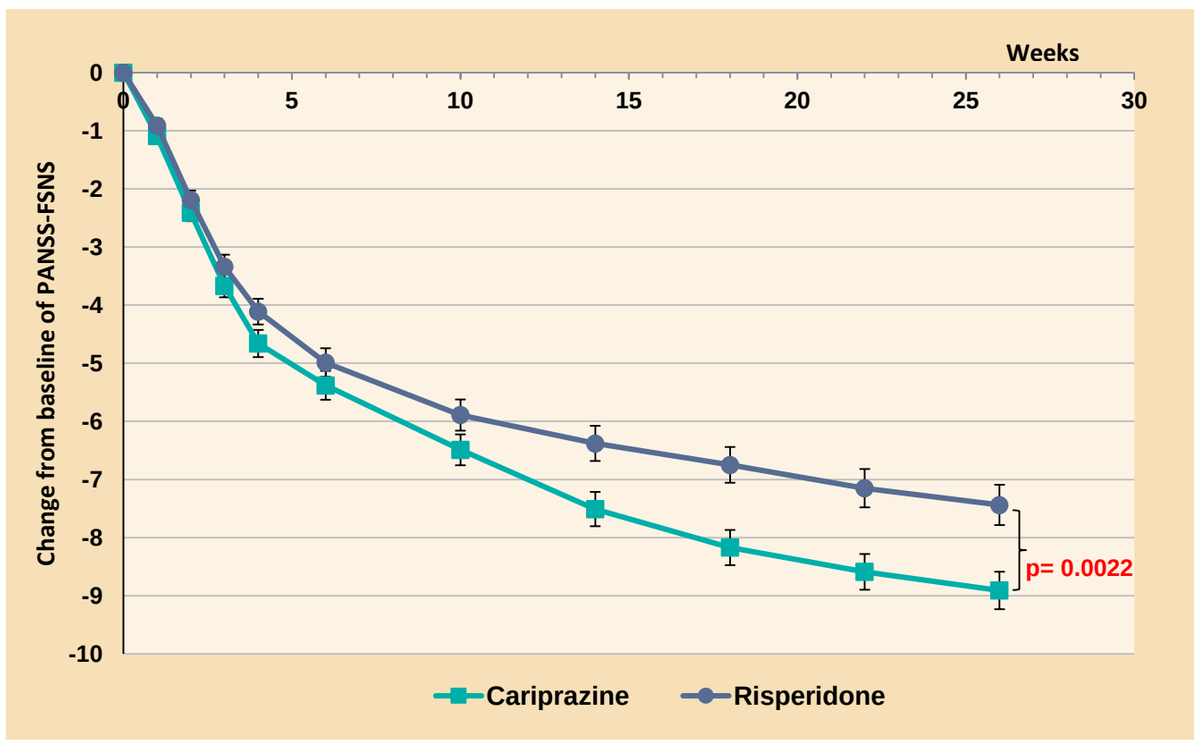
- Efficacy measures were analyzed using a mixed-effects model for repeated measures (MMRM) in the intent-to-treat (ITT) population.

RESULTS

Study-1 (Németh et al., 2017)

- Study-1 (n=460). The difference in mean change from baseline at week 26 in the PANSS-FSNS was statistically significant for cariprazine (target dose 4.5 mg/day) versus risperidone (target dose 4.0 mg/day) from week 14 onwards (-1.46, p=0.0022)

Figure 1 Study-1: Changes of PANSS-FSNS Over Time



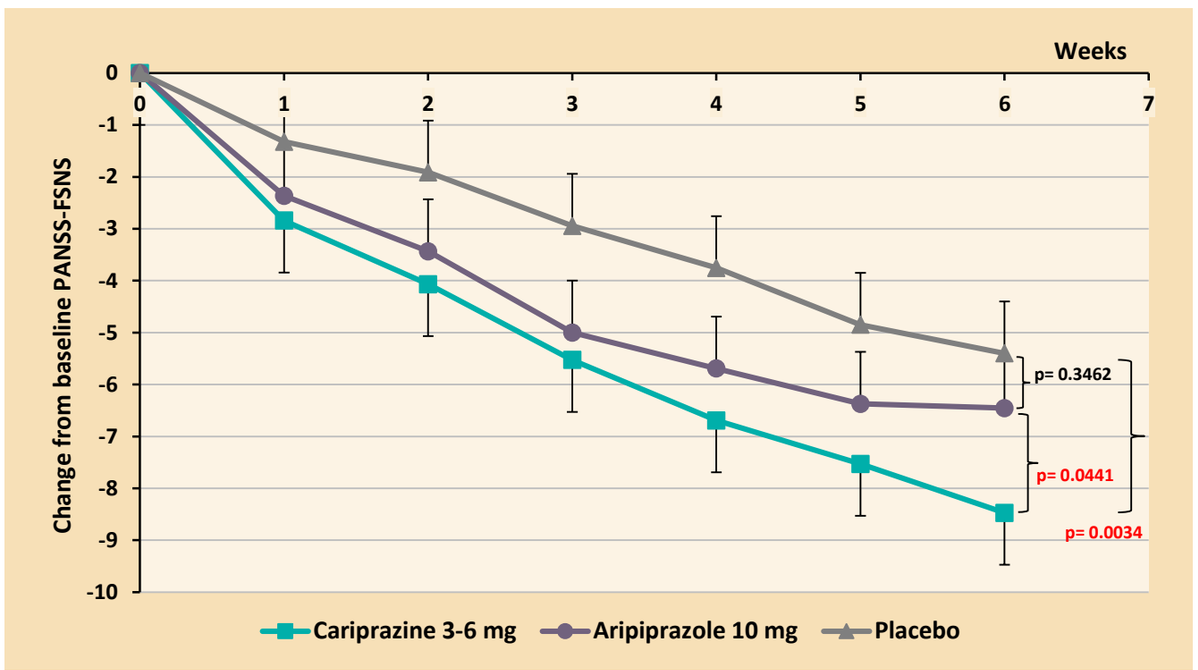
CONCLUSIONS

- **In an adequately designed clinical trial (Study-1) cariprazine proved to be superior versus risperidone in the treatment of predominant negative symptoms of schizophrenia.**
- **Although Study-2 and -3 were not designed to test efficacy in negative symptoms, post-hoc evaluation of these studies provided further evidence of cariprazine's efficacy in predominant negative symptoms.**

Study-2 (Durgam et al., 2015)

- Study-2 (n=112). The difference in mean change from baseline in the PANSS-FSNS was statistically significant for cariprazine versus aripiprazole at Week 6 (-2.02, p=0.0441).
- The difference in mean change from baseline was also statistically significant for cariprazine versus placebo (-3.07, p=0.0034), while the difference for aripiprazole versus placebo was not statistically significant (-1.06, p=0.3462).

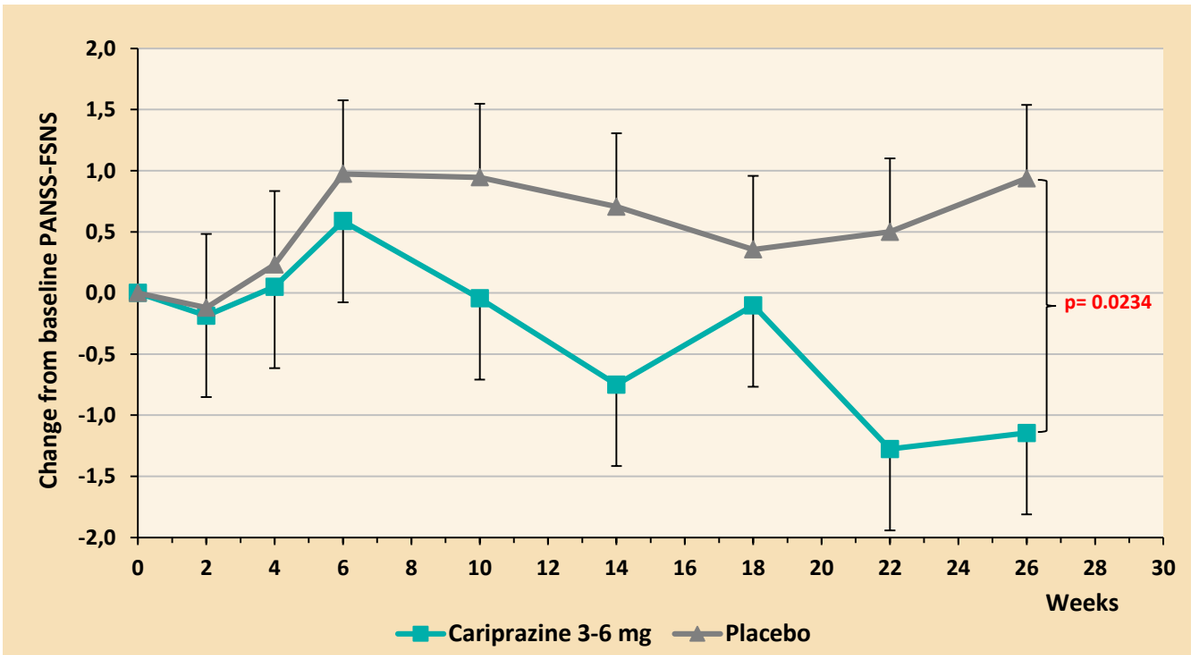
Figure 2 Study-2: Changes of PANSS-FSNS Over Time



Study-3 (Durgam et al., 2016)

- Study-3 (n=20). The difference in mean change from baseline in the PANSS-FSNS was statistically significant for cariprazine versus placebo at Week 26 (-2.08, p=0.0234).

Figure 3 Study-3: Changes of PANSS-FSNS Over Time



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