Safety profile of cariprazine: Post hoc analysis of safety parameters of pooled cariprazine schizophrenia studies

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INTRODUCTION

- Long-term treatment with antipsychotic agents is indicated for all patients with schizophrenia.
- Antipsychotic drugs can be of great benefit for a range of symptoms, but treatment is associated with unpleasant side effects, which contribute to discontinuation and adherence problems [1].
- Choosing the right therapy for patients is crucial and requires different antipsychotic agents with different side effect profiles. Understanding the safety profile of a drug is therefore critical.
- Cariprazine is a potent dopamine D3/D2 receptor partial agonist approved by EMA for the treatment of schizophrenia and by FDA for the treatment of schizophrenia and manic or mixed episodes associated with bipolar I disorder.

STUDY OBJECTIVE

- The aim is to summarize safety data (adverse events, relevant laboratory and vital signs data) of cariprazine in the approved therapeutic dose-range versus placebo in patients with schizophrenia in order to characterize the safety profile of cariprazine.

METHODS

- Pooled data from 2048 cariprazine (CAR 1.5-6 mg) and 683 placebo (PLB) treated patients from eight Phase 3, schizophrenia studies (including 4 short-term 6-week NCT00404573 [RGI-MD-03], NCT00694707 [RGI-MD-16], NCT01104766 [RGI-MD-04], NCT01104779 [RGI-MD-05], 1 long-term 26-week EudraCT 2012-005485-36 [RGI-188-005], 2 long-term 48-week NCT00839852 [RGI-MD-17], NCT01104792 [RGI-MD-11], and 1 long-term up to 92-week NCT01412060 [RGI-MD-06] studies) were analyzed.
- Safety measures included assessment of adverse events (AEs), clinical laboratory values, physical examinations, EPS, depression, and suicidality ratings. Safety parameters were summarized using descriptive statistics.

RESULTS

- The most frequent adverse events with cariprazine (defined as an incidence rate higher than 10%) were akathisia, insomnia and headache; however insomnia and headache occurred in comparable rates also in the placebo group. (Figure 1)

CONCLUSIONS

- Cariprazine was generally safe and well tolerated. The most frequent adverse events were akathisia and EPS, which were mostly mild to moderate in intensity and rarely led to study discontinuation.
- Cariprazine was metabolically silent (metabolic parameters changed similarly to placebo) and had relatively small effects on weight, sedation and QT parameters. Cariprazine does not cause hyperprolactinemia and therefore causes little sexual dysfunction.
- It is a good alternative therapy option for patients suffering from schizophrenia.

Table 1 Management of EPS Including Akathisia

<table>
<thead>
<tr>
<th>Rate of patients with EPS who</th>
<th>Placebo</th>
<th>Cariprazine 1.5 - 6 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>- received anti-EPS medication</td>
<td>50.0%</td>
<td>52.4%</td>
</tr>
<tr>
<td>- had their study drug down-titrated due to EPS</td>
<td>0%</td>
<td>27.6%</td>
</tr>
<tr>
<td>- discontinued the study due to EPS</td>
<td>0%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

Table 2 Incidence of Adverse Events Often Observed with Antipsychotic Treatment

<table>
<thead>
<tr>
<th>Weight gain</th>
<th>Placebo</th>
<th>Cariprazine 1.5 - 6 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean increase from baseline to end in body weight</td>
<td>0.9 kg</td>
<td>1 kg</td>
</tr>
<tr>
<td>Potentially clinically significant weight gain (≥7%) at the end of treatment</td>
<td>3.9%</td>
<td>9.2%</td>
</tr>
</tbody>
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Metabolic parameters

- Shift from normal to high values of fasting glucose at the end of treatment
- Shifts from normal to high values of cholesterol during treatment
- Shifts from normal to high values of triglycerides during treatment

Hormonal side effects

- Decrease in prolactin levels at the end of treatment
- -8.2 ng/ml | -12.9 ng/ml
- Sexual dysfunction | 0.3% | 1%
- Other
- Sedation | 3.1% | 3.7%
- Shifts from normal to high values of QTcB | 3.1% | 3.2%
- Suicidality (ideation and behavior) | 0.6% | 1.2%

REFERENCES


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