Clinical Global Impression Scores and Number Needed to Treat Outcomes in Patients with Postpartum Depression Treated with the Oral Neuroactive Steroid Zuranolone

Introduction

- Postpartum depression (PPD) is one of the most common medical complications during and after pregnancy.
- In the United States, estimates of new mothers experiencing symptoms of PPD vary by state from 0.7% to 23.5%, with an average of 13.2%.
- PPD is associated with a significant impairment in mother–infant bonding and maternal function, including breastfeeding, and caring for the child, with implications for the child’s health and development.
- Multiple prenatal and biological risk factors have been proposed to play a role in the development of PPD.

Methods

- Women (n=311), ages 18–45, 48-months postpartum, diagnosis with PPD (defined as a major depressive episode with onset in the 3rd trimester or 4–6 weeks postpartum) and a baseline HAMD-17 ≥22, were administered study drug in an outpatient setting.
- Patients were randomised 1:1 to receive zuranolone 30 mg or placebo once daily for 14 days, with 4 days follow-up.
- The change from baseline (CFB) in HAMD-17 at Day 15 was the primary endpoint.
- Secondary endpoints included the CFB in HAMD-17 throughout the trial, CGI-I scores, which measure overall improvement post-treatment, and CGI-S scores, which reflect severity at the time of assessment.
- Treatment-emergent adverse events (TEAEs) were assessed throughout the study.
- Post hoc analyses assessed response and remission rates (see tables in the ‘CGI-I and CGI-S Response and Remission Criteria’ section below) defined as scores ≤2 (‘much improved’) or ≤1 (‘very much improved’) for CGI-I, ‘moderately mentally ill’ (rating of 70% normal, not at all’ for CGI-S), respectively, for both the CGI-I and CGI-S scales.
- NNT was calculated using the proportion of CGI-I and CGI-S responders or remitters in each treatment arm at Day 15 and Day 45.
- CGI-I and CGI-S scores and remission rates were assessed using generalized estimating equations models for repeated measures.
- Secondary endpoints and post hoc analyses were not adjusted for multiplicity.

CGI-I AND CGI-S RESPONSE AND REMISSION CRITERIA

<table>
<thead>
<tr>
<th>CRITERION</th>
<th>SUMMARY</th>
<th>RESPONSE</th>
<th>REMISSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-I Response</td>
<td>CGI-I score ≤2 (‘much improved’) or ≤1 (‘very much improved’)</td>
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<tr>
<td>CGI-I Remission</td>
<td>CGI-I score ≤1 (‘very much improved’)</td>
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<tr>
<td>CGI-S Response</td>
<td>CGI-S score ≤2 (‘moderately mentally ill’ or ‘normal, not at all’)</td>
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<tr>
<td>CGI-S Remission</td>
<td>CGI-S score ≤1 (‘moderately mentally ill’ or ‘normal, not at all’)</td>
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Results

- The zuranolone and placebo arms included 76 and 74 patients, respectively, who were randomized and included in the efficacy analyses.
- Baseline demographics and patient characteristics were well balanced between the two treatment arms and have been described in detail previously.1
- Zuranolone was generally well-tolerated, as previously described.2
- The most common TEAE occurring in ≥5% of patients who received zuranolone were somnolence, headache, diarrhea, upper respiratory tract infection, diarrhea, and sedation.

Conclusions

- Zuranolone treatment in patients with PPD has previously been shown to provide rapid (HAMD-17 total score reduction of 70.5% [34.7 points] between Day 0 and 14), consistent improvement in core symptoms of depression.3
- Post hoc analyses show that zuranolone achieved significantly greater improvements in CGI-I and CGI-S remission rates of 73.4% and 62.7%, respectively, compared with placebo (p=0.0334).4
- Single-digit NNTs support the robustness of the observed zuranolone effect.
- CGI-I and CGI-S remission at Day 15 and Day 45 support the robustness of the observed zuranolone effect.

SIGNIFICANTLY HIGHER PROPORTION OF PATIENTS ACHIEVED CGI-I RESPONSE OR REMISSION WITH ZURANOLONE VS PLACEBO

| GRAPH 1 |
|---|---|
| **Zuranolone (N=76)** | **Placebo (N=74)** |
| **Day 15** | **Day 45** | **Day 15** | **Day 45** |
| **Zuranolone** | **Placebo** | **Zuranolone** | **Placebo** |
| **NNT: 1** | | | |

SUPPORT & DISCLOSURES

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