An Updated Meta-Analysis of the Clinical Utility of Combinatorial Pharmacogenomic Testing for Adult Patients with Depression

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Background

- Combinatorial pharmacogenomic (PGx) testing may be a valuable tool to improve clinical outcomes for patients with major depressive disorder (MDD) who have failed at least one treatment.
- An updated meta-analysis was conducted on prospective studies utilizing a commercially available combinatorial PGx test to compare PGx-guided care to unguided care in adult patients with MDD.

Design

- This updated meta-analysis builds upon Brown et al. 2020 (PMID: 32201846), which included 1,550 patients from 4 combinatorial studies.
- Brown et al. demonstrated that care guided by combinatorial PGx testing significantly improved outcomes for patients with MDD compared to unguided care.
- This updated meta-analysis included studies with additional criteria to include additional depression scales.
- A random-effects model was used to calculate the pooled relative risk (RR) of response and remission across all included studies and a subset of randomized controlled trials. A random-effects model was used in this subset because these studies use different depression scales.

Results

Table 1. Summary of Studies Evaluating the Combinatorial PGx Test in Adults with MDD

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Depression Scale</th>
<th>Study Design</th>
<th>Risk Ratio RR 95%-CI Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gedman et al. 2013 10852754</td>
<td>1,541 (baseline)</td>
<td>HAM-D17</td>
<td>8-week, patient- and race-blinded, randomized, controlled trial, open-label extension (24 weeks)</td>
<td>1.41 [1.19; 1.66] 100.0%</td>
</tr>
<tr>
<td>Hall-Flavin et al. 2012 124018772</td>
<td>92 (baseline)</td>
<td>PHQ-9</td>
<td>2-week, open-label study</td>
<td>1.32 (complete week 8)</td>
</tr>
<tr>
<td>Hall-Flavin et al. 2013 23047243</td>
<td>227 (baseline)</td>
<td>PHQ-9</td>
<td>8-week, open-label study</td>
<td>1.54 (complete week 24)</td>
</tr>
<tr>
<td>O'Reilly et al. 2022 15383423</td>
<td>1,658 (randomized)</td>
<td>PHQ-9</td>
<td>24-week, pragmatic, patient- and clinician-unblinded, randomized controlled trial; follow-up for unguided at 36 weeks (after resuming results at 24 weeks)</td>
<td>1.41 (baseline)</td>
</tr>
<tr>
<td>Tiwari et al. 2020 24229738</td>
<td>371 (baseline)</td>
<td>PHQ-9</td>
<td>8-week, patient- and race-blinded, randomized, controlled trial, open-label extension (36 weeks)</td>
<td>1.97 [1.05; 3.72] 100.0%</td>
</tr>
<tr>
<td>Winner et al. 2013 2019</td>
<td>53 (baseline)</td>
<td>PHQ-9</td>
<td>10-week, patient and rater-blinded, randomized controlled trial; open-label extension through 52 weeks</td>
<td>1.40 [1.16; 1.70] 100.0%</td>
</tr>
</tbody>
</table>

Figure 1. All Prospective Studies: Forest plot of 6 prospective studies meta-analyzed for response (A) and remission (B) using random-effects model to assess clinical utility of combinatorial PGx testing for adult patients with MDD.

Figure 2. Randomized Controlled Trials: Forest plot of 4 prospective randomized controlled trials meta-analyzed for response (A) and remission (B) using random-effects model to assess clinical utility of combinatorial PGx testing for adult patients with MDD.

Overall, 3,532 patients were included from six studies, with outcomes evaluated at week 8 or week 10 (Table 1). These studies were in patients who experienced at least one prior treatment failure.

Clinical outcomes were significantly improved for patients with MDD whose care was guided by the combinatorial PGx testing results compared to unguided care (Figure 1: response RR=1.30, 95% CI: 1.16–1.47, p<0.001; remission RR=1.41, 95% CI: 1.19–1.66, p<0.001).

When the four randomized controlled trials were meta-analyzed, patients with MDD had significantly improved outcomes when care was guided by the combinatorial PGx testing results compared to unguided care (Figure 2: response RR=1.32, 95% CI: 1.19–1.47, p<0.001; remission RR=1.41, 95% CI: 1.19–1.66, p<0.001).

The Oslin et al. 2022 study had a design that was different from the others, notably use of PHQ-9 instead of HAM-D17 depression scale. Excluding this study from the overall meta-analysis had similar results: response RR=1.35, 95% CI: 1.15–1.59, p<0.001; remission RR=1.50, 95% CI: 1.20–1.87, p<0.001.

Conclusions

- Access to a combinatorial PGx test improved response and remission rates among adult patients with MDD who experienced at least one prior treatment failure.
- These findings further demonstrate the clinical utility of combinatorial PGx testing for the treatment of MDD and suggest that health care providers may observe significantly increased response and remission rates when using combinatorial PGx testing to inform medication selection in patients with MDD and one treatment failure.