Combinatorial Pharmacogenomic Testing Improves Outcomes for Patients Taking Medications with Gene-Drug Interactions in a Randomized, Controlled Trial

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INTRODUCTION

- Treatment decisions guided by combinatorial pharmacogenomic (PGx) testing may improve outcomes for patients with major depressive disorder (MDD), with the greatest potential improvement expected for patients who are likely failing their current medication(s) due to gene-drug interactions.
- The **G**enomics **U**sed to **I**mprove **DE**presssion **D**ecisions (GUIDED) randomized, controlled trial demonstrated that combinatorial PGx testing significantly improved the rate of response (p=0.007) and remission (p=0.005) and approached significance for symptom improvement (p=0.069).
- However, findings from the GUIDED trial may have been diluted by the inclusion of patients taking medications with no predicted gene-drug interactions at baseline.[1]
- Here, we examined outcomes only in patients who entered the GUIDED trial taking medications with predicted gene-drug interactions.

METHODS

- Patients diagnosed with MDD and an inadequate response to ≥1 psychotropic medication were randomized to treatment as usual (TAU) or to the combinatorial PGx testing-guided arm (guided-care).
  - Combinatorial PGx testing was performed for all patients.
  - All patients and raters were blinded to study arm until after week 8.
  - Physicians were blinded to test report for patients in TAU until after week 8.
- Medications on the combinatorial PGx test report were categorized based on the level of predicted gene-drug interactions:
  - No gene-drug interaction
  - Moderate gene-drug interactions
  - Significant gene-drug interactions
- Only patients taking ≥1 medication(s) subject to moderate or significant gene-drug interactions at baseline were included (N=787).
- Week 8 outcomes were assessed using the 17-item Hamilton Depression Rating Scale (HAM-D17) and the core depression symptom-focused HAM-D6:
  - Symptom Improvement: Percent decrease in score
  - Response: ≥50% decrease in score
  - Remission: HAM-D6 ≤4 or HAM-D17 ≤7

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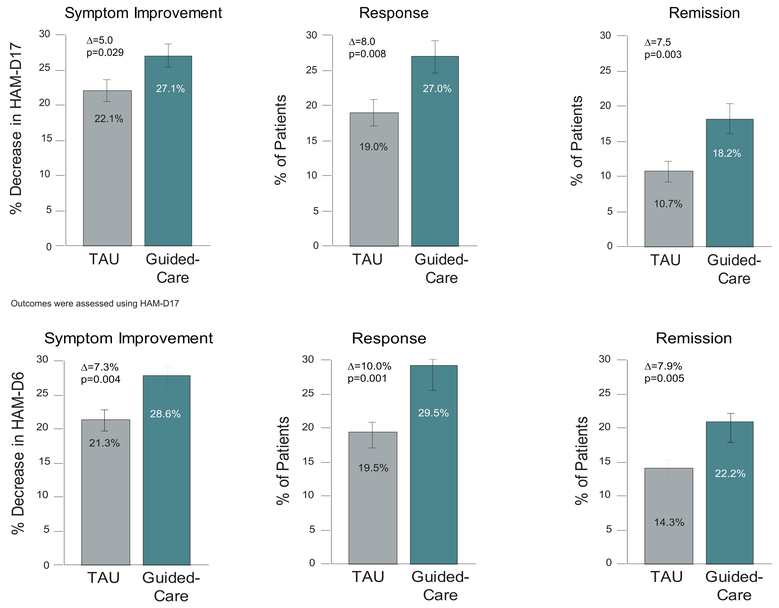
RESULTS

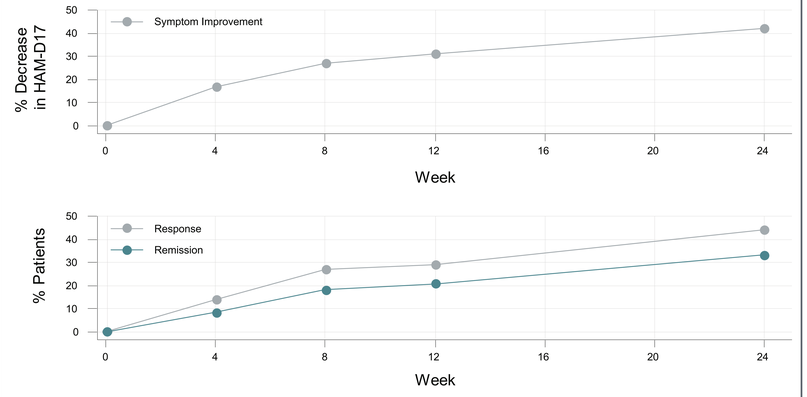
- Among patients taking medication(s) predicted to have moderate or significant gene-drug interactions at baseline, week 8 outcomes based on HAM-D17 were significantly better for those in the guided-care arm compared to TAU (Figure 1).
- Similar findings were observed using the HAM-D6 scale, with larger differences in the guided-care and TAU arms (Figure 1).

Figure 1. Outcomes at week 8 for patients taking medications with gene-drug interactions at baseline



- Patient outcomes in guided-care were durable over the 24-week study (Figure 2).

Figure 2. Durability of improvements in patient outcomes through week 24 for patients in the guided-care arm who were taking medications with predicted gene-drug interactions at baseline



CONCLUSION

- For patients who entered the GUIDED trial taking medications subject to moderate or significant gene-drug interactions, all outcomes were significantly improved when treatment was guided by combinatorial PGx.
- Enhanced improvement was observed using the core depression symptom-focused HAM-D6 scale compared to the full HAM-D17 assessment.
- Overall, these data support the clinical utility of combinatorial PGx for patients with MDD who are likely failing their medication(s) for genetic reasons.

REFERENCES

1. Greden JF., Parikh SV., Rothschild AJ., et al. *Journal of Psychiatric Research*. 2019: 111; 59-67.