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

Michael E. Thase, MD 1; Sagar V. Parikh, MD 2; Gautham Kartha, MD 3; Anthony J. Rothschild, MD 4; Boadie W. Dunlop, MD 5; Charles Debattista, DMH, MD 6; Charles R. Conway, MD 7; Brent P. Forester, MD, MSc 8; Francis M. Mondimore, MD 9; Richard C. Shelton, MD 10; Lisa Brown, PhD 11; Krystal Brown, PhD 12; Matthew Macaluso, DO 11; James Li, PhD 11; Gautham Kartha, MD 3

1. Perelman School of Medicine of the University of Pennsylvania and the Corporal Michael Crescenz VAMC, Philadelphia, PA; 2. University of Michigan Comprehensive Depression Center and Department of Psychiatry, Ann Arbor, MI; 3. Johns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, Baltimore, MD; 4. Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences, Atlanta, GA; 5. Stanford University School of Medicine, School of Medicine, Department of Psychiatry and Behavioral Sciences, Stanford, CA; 6. McLean Hospital, Division of Geriatric Psychiatry, Belmont, MA; Harvard Medical School 7. Johns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, Baltimore, MD; 8. The University of Alabama at Birmingham, Department of Psychiatry and School of Medicine, Birmingham, AL; 9. University of Kansas School of Medicine-Wichita, Department of Psychiatry and Behavioral Sciences, Wichita, KS; 10. Myriad Genetics, Inc., Salt Lake City, UT

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 Genomics Used to Improve Depression Outcomes (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. 9

- 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.

- 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).

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).

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

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) due to genetic reasons.

REFERENCES