Defining and Measuring Safety of Combinatorial Pharmacogenomic Testing for Patients with Major Depressive Disorder (MDD)

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OBJECTIVE

- Pharmacogenomic (PGx) tests are increasingly used to guide medication prescribing in MDD. While efficacy of PGx is promising, the potential for patient harm should be assessed. Here, we use data from the GUIDED trial to evaluate the safety of using the GeneSight test to guide treatment decisions, looking specifically for evidence of patient harms after medications changes are made.

METHODS

COHORT

- GUIDED was a patient- and rater-blinded, randomized, controlled trial including patients diagnosed with MDD who had an inadequate response to ≥1 psychotropic medication.
- All patients received combinatorial pharmacogenomic testing and medications were categorized according to the level of predicted gene-drug interactions (no, moderate, or significant GDI).
- Patients were randomized 1:1 to the combinatorial pharmacogenomic guided-care arm or treatment as usual (TAU). Patients and raters were blinded through week 8. Clinicians were blinded to pharmacogenomic test results for patients in TAU.

ANALYSIS

- Patient harms were defined as:
  - ***Adverse Events*** (AEs, present/absent)
  - ***Worsening Suicidal Ideation*** (increase ≥1 on the HAM-D question)
  - ***Symptom Worsening*** (HAM-D17 increase of ≥1).
- The relative risk of each measure was assessed for patients who changed medications [add and/or drop a medication] and those who made no change.
- Relative risk was also assessed according to medication GDI at baseline and week 8.
  - Relative risk >1 indicates higher risk among patients who made a medication change.

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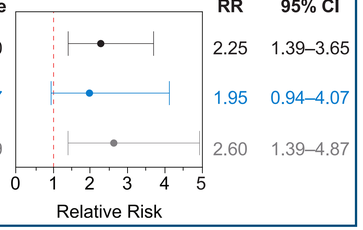
1. Adverse Events

Patients who made a medication change had a significantly increased risk of AEs compared to those who did not, except when medication changes were informed by combinatorial pharmacogenomic testing (guided-care).

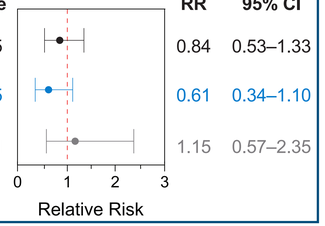
Study Arm	Patients who Experienced AEs: Made a Medication Change	Patients who Experienced AEs: No Medication Change	Δ	p-value	RR	95% CI
Overall N=1,166	17.1%	7.6%	9.5%	0.0010	2.25	1.39–3.65
Guided-Care N=606	16.3%	8.4%	8.0%	0.0737	1.95	0.94–4.07
TAU N=560	17.8%	6.9%	11.0%	0.0029	2.60	1.39–4.87



2. Suicidal Ideation

There were no significant differences in worsening suicidal ideation (SI) among patients who made a medication change compared to those who made no change overall and by study arm.

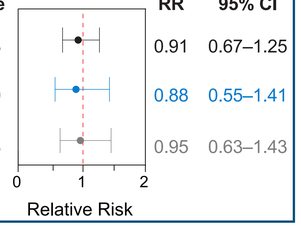
Study Arm	Patients who Experienced Worsening SI: Made a Medication Change	Patients who Experienced Worsening SI: No Medication Change	Δ	p-value	RR	95% CI
Overall N=1,166	7.9%	9.5%	-1.5%	0.4575	0.84	0.53–1.33
Guided-Care N=606	8.9%	14.5%	-5.7%	0.1025	0.61	0.34–1.10
TAU N=560	7.1%	6.2%	0.9%	0.6941	1.15	0.57–2.35



3. Symptom Worsening

There were no significant differences in symptom worsening (SW) among patients who made a medication change compared to those who made no change overall and by study arm.

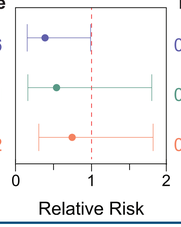
Study Arm	Patients who Experienced SW: Made a Medication Change	Patients who Experienced SW: No Medication Change	Δ	p-value	RR	95% CI
Overall N=1,166	14.5%	15.9%	-1.4%	0.5753	0.91	0.67–1.25
Guided-Care N=606	15.0%	17.1%	-2.0%	0.5950	0.88	0.55–1.41
TAU N=560	14.0%	14.8%	-0.7%	0.8068	0.95	0.63–1.43



4. Patients Taking a Baseline Medication with Significant GDI

Among patients taking ≥1 medication with significant GDI at baseline, those who changed to only medications with no/moderate GDI by week 8 were at lower risk for AEs.

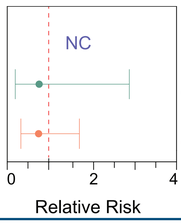
	Changed to taking only meds. with no/moderate GDI by week 8 (N=77)	Taking ≥1 med. with significant GDI by week 8 (N=136)	Δ	p-value	RR	95% CI
Patients who Experienced AEs	6.6%	17.1%	-10.5%	0.0476	0.39	0.15–0.99
Patients who Experienced SIs	5.7%	10.5%	-4.8%	0.3181	0.54	0.16–1.80
Patients who Experienced SW	8.9%	11.9%	-3.0%	0.5232	0.75	0.31–1.82



5. Patients Taking Baseline Medications with No GDI

Among patients taking only medications with no GDI at baseline, there were no significant differences in risk of worsening suicidal ideation or symptom worsening regardless of medication GDI by week 8.

	Changed to taking ≥1 med. with significant GDI by week 8 (N=14)	Taking only meds.with no/moderate GDI by week 8 (N=291)	Δ	p-value	RR	95% CI
Patients who Experienced AEs	16.0%	0.0%	16.0%	N/A	N/A	N/A
Patients who Experienced SIs	11.0%	14.5%	-3.5%	0.6817	0.76	0.20–2.86
Patients who Experienced SW	15.6%	21.3%	-5.7%	0.4644	0.73	0.33–3.86



CONCLUSION

- There was no increased patient harm when combinatorial pharmacogenomic testing was used to inform treatment decisions.
- For patients with significant GDI, patient safety may be improved when treatment decisions align with the combinatorial pharmacogenomic test results.
- This indicates that combinatorial pharmacogenomic testing can be adopted safely into clinical practice without increasing the risk for adverse clinical outcomes.

AFFILIATIONS

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