Prevalence of Pharmacogenomic Actionability in >11,000 Patients Receiving Psychiatric Care

Sarah Morris[1], Joe Stanton,[2] Marcus Badgeley[2], Jai Patel[1]
[1] Levine Cancer Institute, Atrium Health, Charlotte, NC, [2]Tempus Labs, Chicago, IL

Atrium Health
TEMPUS
Poster 92

INTRODUCTION

- Less than 40% of patients with major depressive disorder (MDD) achieve clinical remission after first-line antidepressant treatment.
- Pharmacogenomic (PGx) testing may improve drug selection and/or dosing in patients with genetic variation(s) altering pharmacokinetics through CYP2D6 and CYP2C19.

Primary objective:

- To evaluate the prevalence of PGx actionability in a large, real-world cohort of patients receiving psychiatric care who were referred for clinical PGx testing via Tempus nP.

METHODS

- *CYP2D6* and *CYP2C19* phenotypes were retrospectively evaluated across de-identified records of patients who received Tempus nP PGx testing through routine psychiatric care (N=11,833).
- "Potentially actionable phenotypes" = phenotypes associated with Clinical Pharmacogenomics Implementation Consortium (CPIC)[1,2] or Food and Drug Administration (FDA) PGx guidelines[3] for psychotropics.
- "Clinically actionable phenotypes" = phenotypes associated with medications prescribed prior to testing or considered at the time of testing.
- The impact of *CYP2D6* copy number variant (CNV) allele assignment on phenotype was also assessed.

RESULTS

Table 1. Cohort Characteristics

Characteristic		n (%)
Age (median; range)		*29 (13-77)*
Gender		
	Male	7410 (63%)
	Female	4235 (36%)
	N/A	188 (1%)
Diagnosis		
	MDD	4028 (56%)
	GAD	3321 (46%)
	ADHD	1774 (24%)
	BPD	733 (10%)
	PTSD	687 (9%)
	SCZ	49 (1%)
Indication		
Failed at least one prior medication		6303 (53%)
Never received PGx testing		7405 (63%)
Diagnosis of MDD/GAD		7367 (62%)
Refractory moderate to severe depression		3928 (33%)

Table 1. In 11,833 patients undergoing clinical PGx testing the A) most common diagnoses were depression, anxiety, and attention deficit hyperactivity disorder. B) Sixty-three percent were female and the median age was 29. C) The most common reason for ordering PGx testing was having never received a PGx test prior.

Table 2. CYP2C19/CYP2D6 Phenotypes and Potential Actionability

Phenotype/Actionability	CYP2C19, n (%)	CYP2D6, n (%)
Intermediate Phenotype	3173 (27%)	4637 (39%)
Normal Phenotype	4716 (40%)	6105 (52%)
Poor Phenotype	330 (3%)	694 (6%)
Rapid Phenotype	2733 (23%)	N/A
Ultrarapid Phenotype	881 (7%)	396 (3%)
Potentially actionable*	3944 (33%)	5727 (48%)

*Potentially actionable CYP2C19 phenotypes include poor, rapid, and ultrarapid. Potentially actionable CYP2D6 phenotypes include poor, intermediate, and ultrarapid.

Table 2. Sixty-five percent of patients had actionable phenotypes for CYP2D6 and/or CYP2C19; 48% and 33% of patients had potentially actionable CYP2D6 and CYP2C19 phenotypes, respectively.

Table 3. Medication Prescribing and PGx Actionability

Patient Medication	No. of patients actionable	Fraction actionable	No. of patients
escitalopram	183	0.31	581
citalopram	69	0.33	211
amitriptyline	40	0.66	61
doxepin	23	0.58	40
sertraline	21	0.03	732
aripiprazole	20	0.05	434
venlafaxine	19	0.06	324
dextroamphetamine/amphetamine	17	0.05	349
clomipramine	16	0.64	25
nortriptyline	14	0.41	34

Fraction actionable
0.00 0.25 0.50 0.75 1.00

Table 3. Combines medications reported as attempted and being considered. Of 865 patients who attempted medications related to CYP2D6 and/or CYP2C19, 22% (n=187) had at least one actionable phenotype. Of 1,141 patients considering medications related to CYP2D6 and/or CYP2C19, 18% (n=205) had at least one actionable phenotype.

Figure 1. Most common CNV Diplotypes

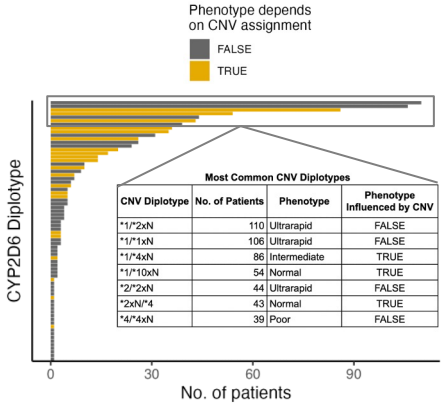

Fig 1. Of 883 patients with *CYP2D6* CNVs (7.5% overall), 369 patients (42% of all patients with CNVs) had genotypes in which knowledge of allele-specific CNVs would change the phenotype (most often *1/*4, *1/*10, and *2/*4).

CONCLUSIONS

- The prevalence of *CYP2D6* and *CYP2C19* actionability is high in a large real-world cohort of patients receiving psychiatric care and referred for clinical PGx testing.
- Comprehensive genotyping, including allele-specific CNVs for CYP2D6, is critical for accurate phenotype assignment and can identify clinically significant drug-gene interactions in psychiatric care.

Acknowledgements: This wonderful collaboration was supported by Atrium Health's PGx expertise and Tempus Labs' research infrastructure and scientific writing (Matthew Kase).

References

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