

GeneSight® Psychotropic Case Study

Cry For Help: 96 Year Old with Alzheimer's Disease with Behavioral Disturbances and Depression

Background

Behavioral health drug selection and dosing is a trial and error process that often leads to delayed response time, frustration and increased medical costs. There is a high degree of variability in response to behavioral health medications, some of which is due to individual genetics. Assurex Health utilizes its GeneSight® pharmacogenomic technology to understand how unique inherited traits might influence a patient's response to medication. GeneSight Psychotropic is a pharmacogenomic test developed to help clinicians select medications commonly prescribed to treat behavioral health conditions. There have been multiple studies published in peer reviewed journals addressing the clinical utility of the GeneSight Psychotropic test.¹⁻⁴

Patient

- 96 year old Caucasian female with Alzheimer's disease with behavioral disturbances and depression.
- She was previously discharged from multiple long term care communities due to constant escape and exit seeking behavior.
- She would escape from the facility, run into traffic, knock on neighboring houses, and scream for help. She also consistently exhibited loud behavioral outbursts and severe agitation.
- Past medical history: High blood pressure, which has been appropriately monitored and treated
- Social history: No known problems with alcohol, nicotine, or illicit drugs
- Previous psychiatric medication trials: Unknown as records were not transferred from previous care facility
- Medications at the time of GeneSight testing: levetiracetam (Keppra®) 500 mg/d, escitalopram (Lexapro®) 20 mg/d, and memantine (Namenda®) 5 mg/d
- The GeneSight test was then ordered to utilize pharmacogenomic information to help support the next steps in treatment.

GeneSight® Psychotropic Results

ANTIDEPRESSANTS

USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION	SIGNIFICANT GENE-DRUG INTERACTION
desvenlafaxine (Pristiq®) levomilnacipran (Fetzima®) vilazodone (Viibryd®)	amitriptyline (Elavil®) 1 bupropion (Wellbutrin®) 1 clomipramine (Anafranil®) 1 desipramine (Norpramin®) 1 doxepin (Sinequan®) 1 duloxetine (Cymbalta®) 1 fluvoxamine (Luvox®) 1 mirtazapine (Remeron®) 1 nortriptyline (Pamelor®) 1 selegiline (Emsam®) 1 venlafaxine (Effexor®) 1 vortioxetine (Trintellix®) 1 trazodone (Desyre®) 3 citalopram (Celexa®) 4 escitalopram (Lexapro®) 4 sertraline (Zoloft®) 4 paroxetine (Paxil®) 1,4 imipramine (Tofranil®) 1,6	fluoxetine (Prozac®) 1,6

CLINICAL CONSIDERATIONS

- 1: Serum level may be too high, lower doses may be required.
- 3: Difficult to predict dose adjustments due to conflicting variations in metabolism.
- 4: Genotype may impact drug mechanism of action and result in reduced efficacy.
- 6: Use of this drug may increase risk of side effects.

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GeneSight® Psychotropic Results (continued)

The patient's genetic results for each of the 12 genes was identified as:

CYP1A2	Extensive (Normal) Metabolizer	-246T>DEL - T/DEL, -163C>A - C/A
CYP2B6	Intermediate Metabolizer	*1/*6
CYP2C19	Extensive (Normal) Metabolizer	*4/*17
CYP2C9	Intermediate Metabolizer	*1/*2
CYP3A4	Extensive (Normal) Metabolizer	*1/*1
CYP2D6	Intermediate Metabolizer	*1/*4
UGT1A4	Extensive (Normal) Metabolizer	*1/*1
UGT2B15	Intermediate Metabolizer	*2/*2
SLC6A4	Intermediate Response	L/S
HTR2A	Normal Sensitivity	G/A
HLA-B*1502	Lower Risk	Not Present
HLA-A*3101	Lower Risk	A/A

Pharmacogenomic Insight

The "short" and "long" form of the promoter of the gene that encodes the serotonin transporter is one of the most studied pharmacodynamic genes in psychiatric pharmacogenomics. Meta-analyses have shown a poorer response for individuals who have one or two "short" variants and possible increased risk of side effects. In addition to the pharmacodynamic issues with escitalopram, the patient also had pharmacokinetic issues given her intermediate metabolizing phenotype at the CYP2D6 pathway. While the intermediate metabolizer phenotype at CYP2D6 would potentially not impact a pediatric or middle-aged patient's response to escitalopram, CYP enzyme production decreases with age. This reduction in CYP activity could possibly exacerbate the patient's genetic predisposition to metabolize poorly through the CYP2D6 pathway and potentially cause additional side effects. For these reasons, the clinician chose to discontinue escitalopram for his geriatric patient.

MEDICATIONS AT TESTING	CHANGE IN MEDICATIONS
levetiracetam (Keppra®) 500 mg/d	Discontinued levetiracetam (Keppra®)
escitalopram (Lexapro®) 20 mg/d	Discontinued escitalopram (Lexapro®)
memantine (Namenda®) 5 mg/d	memantine (Namenda®) maintained

Pharmacogenomic-Informed Decision Making

- Prior to receiving the GeneSight results, the healthcare provider realized that levetiracetam (Keppra®) may have been contributing to the patient's behavioral issues as several possible side effects of the medication were changes in mood or behavior including irritability and aggression. As the patient has no known history of epilepsy, levetiracetam (Keppra®) was immediately discontinued. However, this failed to improve any of the patient's behavioral symptoms.
- Following GeneSight testing, it was noted that the patient's current psychiatric medication, escitalopram, was categorized into the yellow ("Moderate Gene-Drug Interaction") category with a footnote warning that "genotype may impact drug mechanism of action and result in reduced efficacy". As the patient's genetic makeup made the patient less likely to respond to escitalopram, and more likely to have side effects, the healthcare provider then chose to titrate the patient off this medication.

Conclusions

- After the GeneSight test informed treatment, the patient experienced an immediate cessation of behavioral outbursts. There were no additional attempts to escape the facility or instances of howling or yelling. Instead, the patient began to interact with other residents of the long term care facility in a pleasant, friendly, and helpful manner.
- The healthcare provider shared that without the GeneSight test the patient would mostly likely have been given additional medications, such as antipsychotics, to try and reduce behavioral outbursts. Instead, the GeneSight test allowed the facility to reduce the number of medications the patient was taking.
- Additionally, the healthcare provider notes that the patient has a much better quality of life now and seems to be at peace. The provider describes GeneSight as a test that "saved" both the patient and this facility. Prior to using the GeneSight test, treatment staff had to follow the patient around all day to prevent her from escaping and having behavioral outbursts in the streets.
- Following the improvement in the patient's demeanor after GeneSight testing, her son remarked "imagine how much better her life could have been if we'd done this years ago!"