GeneSight® ADHD Case Study

Reducing the Cycle of Frustration: 15 year old with Attention-Deficit/Hyperactivity Disorder

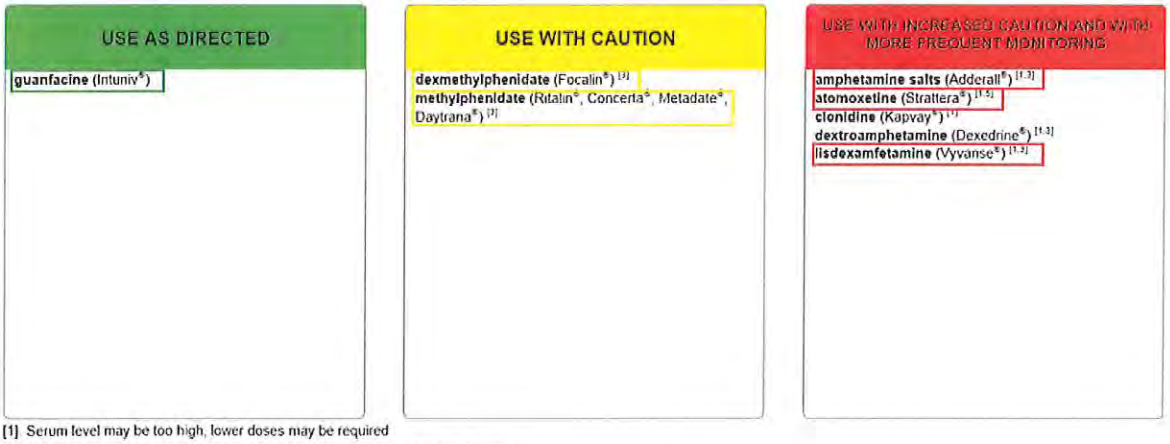
Background

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 ADHD is a pharmacogenomic test developed to help clinicians select medications commonly prescribed to treat behavioral health conditions.

Patient

- The patient is a 15 year old male with a history of congenital muscular dysplasia who presents to a developmental pediatric practice with ADHD symptoms
- The patient's target symptoms include: inattention, anxiety, distractibility, and difficulty attenuating visual or auditory stimuli
- Family history of ADHD
- Social history: There was no evidence of substance abuse or misuse
- The patient presented to the clinic at the age of 10 where he was initially treated for attention-deficit/hyperactivity disorder, predominately inattentive type, without the benefit of GeneSight testing
- The patient's medication trial history is as follows:
  - Failed lisdexamphetamine (Vyvanse®) due to becoming anxious and irritable on a relatively low dose
  - Failed dexmethylphenidate ER (Focalin XR®) due to headache and flattened effect
  - Failed methylphenidate ER (Concerta®) due to poor appetite, headache, and flat effect
  - Failed atomoxetine (Strattera®) due to nausea and headache
  - Failed amphetamine/dextroamphetamine (Adderall XR®) due to irritability, loss of appetite, and insomnia
  - Patient was put on guanfacine ER (Intuniv®) which was titrated to 4 mg daily without major side effects
- On guanfacine ER (Intuniv®) the patient had improvement in attention, less distractibility and improved concentration. He also had improvement in functional goals in school, relationships with his family members and social interaction.
- ***GeneSight ADHD was ordered five years later due to complex pharmacology and the patient's trepidation toward any future medication changes.***

GeneSight ADHD Results



[1] Serum level may be too high, lower doses may be required

[3] COMT genotype is associated with reduced therapeutic response to this drug

[5] CYP2D6 genotype indicates that this patient may experience increased side-effects, but also increased efficacy

GeneSight® ADHD Case Study

Reducing the Cycle of Frustration: 15 year old with Attention-Deficit/Hyperactivity Disorder

GeneSight ADHD Results (continued)

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

CYP2D6	Poor Metabolizer	*5/*6
COMT	Reduced Activity	MET/MET
ADRA2A	Typical Response	G/G

Pharmacogenomic Insight

This individual is homozygous for the Met variant of COMT. Homozygous Met carriers are thought to have more dopamine and norepinephrine available in the prefrontal cortex (PFC) due to decreased metabolism of these catecholamines. Several studies have shown COMT Met homozygotes to have reduced response to stimulant medications, which act to increase catecholamines in the PFC. Additionally, regarding metabolism, FDA prescribing information identifies CYP2D6 poor metabolizers as likely to have more side effects with atomoxetine.

Pharmacogenomic-Informed Decision Making

- In reviewing the GeneSight ADHD results, the physician notes the current and previous medication trials for the patient in relation to the green-yellow-red advisory categories and drug specific footnotes which supply details for the gene-drug interactions:
  - Atomoxetine is found in the red ("use with increased caution and with more frequent monitoring") category with two advisory footnotes: "serum level may be too high, lower doses may be required" and "genotype indicates that this patient may experience increased side-effects, but also increased efficacy."
  - Lisdexamfetamine and amphetamine salts (Adderall) are found in the red (use with increased caution and with more frequent monitoring) category with two advisory footnotes: "serum level may be too high, lower doses may be required" and "genotype is associated with reduced therapeutic response to this drug."
  - Methylphenidate and dexmethylphenidate are found in the yellow ("use with caution") category with the advisory footnote, "genotype is associated with reduced therapeutic response to this drug."
  - Guanfacine is found in the green ("use as directed") category suggesting that there is not a known negative gene-medication interaction for guanfacine in this individual.
- The physician notes that the patient's pharmacologic history is remarkably consistent with his GeneSight ADHD information. The patient appeared overstimulated on four traditional stimulant medications and had side effects to atomoxetine. All five medications were found in the yellow or red advisory categories.

Conclusions

The physician states, "This patient is a clear example of how the genetic testing can decrease the number of visits by the patient. I would've probably gone directly to the Intuniv instead of going through 6 different stimulant trials. Since most parents will not give a physician a second or third chance, let alone five or six chances to find the medicine that will help their child focus on what needs to be done; using this genetic testing is not only money saving, it is also conducive to helping the parent feel reassured that their child is on the 'right' medicine."

genesight®