personalized prescribing
next gen pharmacogenetics

Name: [redacted]
Sample ID: WF021004
Physician: [redacted]

Sample Type: Saliva
Received: 24-Jun-24
Reported: 26-Jun-24

175 West Beaver Creek, Unit 24
Richmond Hill, ON L4B 1L1

Rx Report™ - Psychiatry - Anxiety & Depression

Pharmacogenomic Test (Highly Confidential)

Result Summary

Dear Dr. Zaidi,

Wayne Featherbe is diagnosed with anxiety and depression along with some trouble sleeping, as well as neck and back pain. He has sought out a consultation with a clinical pharmacist at Personalized Prescribing Inc. This consultation included a pharmacogenomic test.

The pharmacogenetic test results and our algorithms indicate:

- The initiation of Desvenlafaxine (Pristiq) 50 mg once daily each morning (alternative: Duloxetine (Cymbalta) 30 mg once daily each morning, titrated to effect- may be more helpful if nerve related pain is present)
- The addition of Trazodone 50 mg at bedtime for sleep

Pharmacokinetic Rational:

Level of Evidence: High - (CPIC, DPWG and FDA).

CYP2D6	*1	*1

Normal Metabolizer

According to a high level of evidence, this patient is a CYP2D6 normal metabolizer of Fluoxetine, Fluvoxamine, Paroxetine, Venlafaxine, Duloxetine, and Vortioxetine. This means they have no barriers in clearing these medications from their body and the medication is likely to reach normal bloodstream concentrations. The Clinical Pharmacogenetic Implementation Consortium (CPIC) recommends initiating these medications at their regular starting dose- no dose adjustment is required.

CYP2C19	*1	*1

Normal Metabolizer

According to a high level of evidence, this patient is a CYP2C19 normal metabolizer of Sertraline and Citalopram/Escitalopram. This means they have no challenges breaking down or clearing these medications from their body and the medication is likely to reach normal bloodstream concentrations. The Clinical Pharmacogenetic Implementation Consortium (CPIC) recommends initiating these medications at their regular starting dose- no dose adjustment is required.

This patient has the following Blood Brain Barrier profile:

Level of Evidence: Low.

ABCB1	rs2235015	C	A
ABCB1	rs1045642	G	A
ABCB1	rs2032583	A	A

Moderate Permeability

Tested ABCB1 genes indicate this patient has moderate expression of the p-glycoprotein pump (P-gp) at the blood brain barrier. This pump is responsible for expelling any substance from the brain that it recognizes as foreign. This patient is likely to have moderately favorable brain permeability for most anti-depressants.

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Pharmacodynamic Rational (Brain Receptors)

Level of Evidence: Low (based on published literature)

This patient's gene MAO-A rs1137070 TT among others denote high pre-synaptic enzymatic degradation of neurotransmitters serotonin and norepinephrine (noradrenaline) in the brain and thus relatively lower baseline levels of these neurotransmitters. This indicates that the patient may benefit maximally from targeted treatment with selective reversible MAO-A inhibitor Moclobemide, which is a 2nd line anti-depressant, dosed twice daily. Though effective and well-tolerated, this medication is reserved for use once others have failed. Additionally, previous anti-depressant should be discontinued for at least one week prior to initiation, if previous medication is Fluoxetine, discontinue for 5 weeks prior to initiation of Moclobemide. Other recommended medications above will also increase both serotonin and noradrenaline levels, particularly SNRIs such as Desvenlafaxine as well as Duloxetine, Desvenlafaxine has ten times greater affinity for increasing serotonin relative to noradrenaline, which may be beneficial for anxiety and mood, Duloxetine increases both serotonin and noradrenaline at equal levels, mostly improving depressive and nerve related pain symptoms.

See references at: personalizedprescribing.com/references

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Summary of Psychiatry - Anxiety & Depression medication

The tested genes have resulted in the following outcomes.
See following pages for an interpretation of the table below.

Drug	Metabolism	Efficacy	Side Effects
Amitriptyline, Clomipramine, Imipramine, Trimipramine, and Doxepin	Normal Metabolizer		
Amphetamines	Normal Metabolizer	Moderate Responder	**Nausea** | **Anxiety** | **Appetite Suppression and Insomnia** | **Social Withdrawal**
Atomoxetine	Normal Metabolizer	Moderate Responder	**Anxiety**
Bupropion	Normal Metabolizer	Moderate Responder	**Anxiety**
Citalopram	Normal Metabolizer	Good Responder	**Heart Palpitations** | **Memory Loss/Concentration Problems**
Desipramine	Normal Metabolizer	Good Responder	**Anxiety**
Desvenlafaxine		Good Responder	**Fatigue** | **Anxiety**
Duloxetine	Normal Metabolizer	Good Responder	**Anxiety**
Escitalopram	Normal Metabolizer	Good Responder	**Heart Palpitations** | **Memory Loss/Concentration Problems**
Fluoxetine	Normal Metabolizer	Moderate Responder	**Insomnia**

Fluvoxamine	Normal Metabolizer	Good Responder	**Stomach Upset and Nausea**
Levomilnacipran		Moderate Responder	**Anxiety**
Methylphenidate		Moderate Responder	**Social Withdrawal** | **Nausea** | **Anxiety**
Mirtazapine		Moderate Responder	
Moclobemide		Good Responder	
Nortriptyline	Normal Metabolizer	Moderate Responder	
Paroxetine	Normal Metabolizer	Good Responder	**Nausea - Stomach Upset**
Sertraline	Normal Metabolizer	Good Responder	
Trazodone		Moderate Responder	
Venlafaxine	Normal Metabolizer	Good Responder	**Increased Depression** | **Fatigue**
Vilazodone		Moderate Responder	
Vortioxetine	Normal Metabolizer	Moderate Responder	

Level of Evidence:

Metabolism - High level (CPIC, DPWG and FDA)

Efficacy and Side Effects - Low level (based on published literature.)

Colour Legend:

Green: Indicates high likelyhood of favourable therapeutic effect on a medication and/or a lower incidence of side effects.

Yellow: Indicates likelyhood of partial therapeutic effect on a medication and/or possible incidence of side effects.

Red: Indicates less likelyhood of intended therapeutic effect on a medication and/or high likelyhood of side effects.

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Pharmacogenomics is a two-part process, pharmacokinetics, and pharmacodynamics.

Pharmacokinetics is what the body does to the drug. (Liver enzymes metabolism)

How it absorbs it, metabolizes it to its' active component, circulates it and most importantly, clears it through the liver.

Patients can be one of the following:

Extensive Metabolizers are expected to clear these medications normally.
Intermediate Metabolizers have a slightly reduced ability to clear these medications from the body and may be more sensitive to their dose-related side-effects.
Poor Metabolizers have a significantly reduced ability to clear the medication and could result in serious side effects.
Ultra-Rapid Metabolizers clear these drugs too quickly such that the drug is likely to be ineffective, especially at lower dose ranges.

Pharmacokinetics - blood brain barrier (BBB): The ABCB1 gene codes for the P-gp protein which is embedded in the BBB. It protects the brain by efluxing drugs and antigens from the brain. Many anti-depressants are ‘substrates’ of the blood barrier and are highly prone to expulsion from the brain, limiting efficacy and increasing peripheral side-effect burden.

Bupropion, Trazodone, Mirtazapine, Midazolam, Lamotrigine, Sertraline are considered **non-substrates** and are not easily effluxed by the BBB.
Trimipramine, Amitriptyline, Buspirone, Vortioxetine, Haloperidol, Fluoxetine, Clozapine, Methylphenidate are **moderate substrates** in the order they are stated. They are expelled by the BBB if it is of **high function (low brain permeability).** They are not easily expelled if the BBB is of **lower function (high permeability).**
Venlafaxine, Nortriptyline, Citalopram, Duloxetine, Paroxetine, Fluvoxamine, Escitalopram, Desvenlafaxine, Vilazodone, Levomilnacipran, Risperidone are high substrates in the order they are stated. They are easily effluxed by the blood brain barrier especially if the BBB is of **high or moderate function (low brain permeability).**

Pharmacodynamics is what the drug does to the body.

Drugs have mechanisms of action that include attaching to target genes, and by doing that, they might block their action or might potentiate their action or otherwise.

If most of the target genes are compatibly expressed, the drug is likely to succeed, if some genes are compatible and others are not, the drugs work moderately or may cause side-effects, and if most of the genes are incompatible, the drug fails.

Pharmacodynamics also can indicate side effects: The drug might attach to other genes that are not intended, which results in side effects.

Please do feel free to contact me if you have any questions.

Reported By:
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The Rx Report™ is aimed to provide genetic information to individuals and to their healthcare professionals that may help in selecting the appropriate medications for individuals struggling with mental illness medications. The report is based on patient assessment, including correct diagnosis, clinical history, relevant lifestyle factors, family history, co-morbidities, medications, and other factors. The Result Summary by a pharmacist is derived based on individual's genetic variations (SNPs) that are relevant to drug metabolism, transport, and target receptor binding for efficacy and side effects as per Personalized Prescribing Inc. (PPI) proprietary algorithm.

DISCLAIMER

The result summary is not intended to be diagnostic but to indicate drugs that are more likely to be effective for individuals. Any decision to prescribe or change medications should only be made by individual's treating physician based on their professional judgement and considering patients' medical history and other relevant information available in clinical literature, practice guidelines, FDA-approved drug labelling, indications, warnings, precautions etc.

The genes included in the report are based on the most recent literature available in public platforms such as FDA, Clinical Pharmacogenetic Implementation Consortium (CPIC), PharmGKB, and peer-reviewed medical literature. Any periodic updates on gene-drug interactions by PPI because of continuous changes in the availability of pharmacogenomic information, will be reflected in patients' genetic profiles, however, no updated Result Summary will be sent if not requested by patients or their physicians.

Discussion with PPI Pharmacist

Healthcare professionals/ psychiatrists/ physicians interested in discussing PPI pharmacogenomics testing service, patient report interpretation etc. can contact PPI psychopharmacists. Please send an email to pharmacist@personalizedprescribing.com or call 647-943-0210 ext.1 to schedule an appointment with a psychopharmacist.

Test Methodology

The test was developed and validated in Personalized Prescribing Inc. (PPI) laboratory. PPI uses in-house designed primers and assay reagents from Agena Bioscience, USA to perform the analysis. The test is used for clinical purposes, not for investigational use. Rx Report-Psychiatry & Pain test by PPI has not been approved by the U.S. Food and Drug Administration (FDA).

Variants Tested

CYP2D6 (*1, *2, *3, *4, *6, *7, *8, *9, *10, *14A, *17, *29, *41), CYP2C19 (*1, *2, *3, *4, *4B, *5, *6, *7, *8, *17), ABCB1 (rs2032583, rs2235015, rs1045642), NPY (rs16147), IL1B (rs16944), TNFα (rs1800629), IL-6 (rs1800795), IL-10 (rs1800896), CRHR1 (rs110402), FKBP5 (rs3800373, rs1360780, rs4713916), NR3C1 (rs10052957, rs41423247, rs6198), NR3C2 (rs5522), GAD1 (rs3791850), SLC1A2 (rs3812778), GABAa (rs211037), GRIK4 (rs11218030, rs1954787), GRIN1 (rs4880213), GRIN2B (rs1805247, rs1805502), GRIA1 (rs1994862), IDO (rs9657182), BDNF (rs6265), TPH1 (rs1800532), TPH2 (rs1487278, rs7963803, rs11178997, rs4570625), MAO-A (rs1465107, rs6323, rs1137070), HTR1A (rs6295, rs10042486), HTR1B (rs6296, rs9361233), HTR2A (rs6311, rs6313, rs6314, rs7997012), HTR2C (rs3813929, rs1414334), HTR3A (rs1062613), HTR3B (rs1176744), HTR7 (rs7905446), SLC6A4 (SS/SL/LL and rs255331), TH (rs10770141), DBH (rs1611115, rs2519152, rs1108580), MAO-B (rs1799836), COMT (rs4680), DRD2 (rs1076560, rs1799732, rs1799978, rs1800497), DRD1 (rs4532), DRD3 (rs6280), SLC6A2 (rs2242446), ADARA2A (rs1800544), GNB3 (rs5441, rs5443), CCK (rs1799923), CACNA1C (rs1006737), FAAH (rs324420), ADRB2 (rs1042713), ADM (rs11042725), MC4R (rs17782313, rs489693), MTHFR (rs1801131, rs1801133), ADRB1 (rs1801252, rs1801253), CHRNB2 (rs2072661), SERPINE1 (rs2227631), PDL1M5 (rs2433320), ACE (rs4291), SLC6A3 (rs2550948), SNAP25 (rs3746544), SLC6A2 (rs12708954, rs3785143), ADGRL3 (rs1355368, rs6813183)

PS: Other variants are not included in the test.

Limitation of Test Process

The test methodology has limitations. The quality and quantity of DNA extracted from patients are dependent on saliva sample collection process, for example dietary or microbial influence which can impact the test process. PCR process can be influenced by exogenous enzymes or PCR inhibitors that may affect the assay result. SLC6A4 is a very delicate assay that is developed and validated and interpreted based on currently available scientific evidence. The result interpretation may vary if rs255331 is not considered in addition to Long (L) and Short (S) alleles. There are a couple of SNPs that have repeat bases, amplification of DNA samples can be deterred due to repeat bases. As the test does not include sequencing of whole genome, there could be undetected genetic variants that may influence the phenotype. Non-genetic factors such as drug-drug interactions that are unknown could also limit the interpretation of the test. Rx report- Psychiatry & Pain test report is based on available resources in scientific platforms like PharmGKB, FDA, DPWG and CPIC. PPI geneticists and pharmacists conduct in-house research to understand the clinical relevance of the variant identified, phenotypes, and recurrent risks.

References

There are references for our developed algorithms listed at our website: www.personalizedprescribing.com/references/