Patient Name:	**Dummy**	CRM ID:	**XXX**
Age/DOB:	**81 Years**	Sample Type:	**EDTA Whole Blood**
Sex:	**Male**	Collection Date:	**17/11/2024**
Referring Clinician:	**Dr. XXX**	Receiving Date:	**18/11/2024**
Test Requested:	**Cytochrome P450 2C19 (CYP2C19) Genotyping For Clopidrogrel Resistance**	Reporting Date:	**25/11/2024**

Cytochrome P450 2C19 (CYP2C19) Genotyping For Clopidrogrel Resistance

CLINICAL DIAGNOSIS/SYMPTOMS

HTN, polypectomy colon, memory issues, recurrent episode of seizures

RESULTS

*2/*2 Genotype Detected (Poor metabolizer)

Mutant Allele Nomenclature	CYP2C19*2
mRNA Nomenclature	c.681 G>A
Patient Genotype	Homozygous (G/A)

INTERPRETATION

*2/*2 genotypes detected (An individual with 2 non function alleles) in Dummy which phenotypically signifies Non-functional enzyme activity (i.e. Poor metabolizer). The CYP2C19*2 c.681 G>A homozygous mutation is a loss-of-function allele that results in a nonfunctional protein. An individual who is homozygous for the CYP2C19*2 allele poorly metabolizes CYP2C19 substrates, such as clopidogrel. This can contribute to inter-individual variability in therapeutic response.

Interpretation Guidelines -

Phenotype	Genotype	Examples of diplotypes
Ultrarapid metabolizer	An individual with 2 increased function alleles	*17/*17
Rapid metabolizer	An individual with one normal function allele and one increased function allele	*1/*17
Normal metabolizer	An individual with 2 normal function alleles	*1/*1
Intermediate metabolizer	An individual with one normal function allele and one non function allele or non function allele with one increased function allele	*1/*2 *1/*3 *2/*17 *3/*17
Poor metabolizer	An individual with 2 non function alleles	*2/*2 *2/*3 *3/*3

Total Alleles Assessed-

Allele Designation	Variant	dbSNP	Predicted Enzyme Activity
CYP2C19*1	None	------	Normal
CYP2C19*2	c.681 G>A	rs4244285	Non- functional
CYP2C19*3	c.636 G>A	rs4986893	Non- functional
CYP2C19*17	-806C>T	rs12248560	Increased- functional

Note: The normal version of the gene, written as CYP2C19*1, provides instructions for producing a normally functioning CYP2C19 enzyme. If a person has two copies of the CYP2C19*1 version of the gene in each cell, they are able to convert clopidogrel normally. The two most common CYP2C19 gene polymorphisms associated with clopidogrel resistance CYP2C19*2 and CYP2C19*3 result in the production of a non-functional CYP2C19 enzyme that is unable to activate clopidogrel. CYP2C19*2 polymorphism is associated with non-responsiveness to clopidogrel therapy and the CYP2C19*17 polymorphism enhances antiplatelet activity of clopidogrel. Depending on haplotypes of these two polymorphisms, clopidogrel-treated patients can be protected or not from stent thrombosis and ischaemic events.

METHODOLOGY

Targeted sequencing and mutation analysis was performed by Polymerase Chain Reaction (PCR) followed by automated DNA sequencing of the amplicon using BigDye Terminator Chemistry on an ABI Genetic Analyzer 3500XL platform. Sequencing data were aligned to NCBI database to analyze the mutations.

BACKGROUND

- The gene is located within a cluster of cytochrome P450 genes on chromosome 10q24.
- The CYP2C19 enzyme plays a role in the processing or metabolizing of at least 10 percent of commonly prescribed drugs, including a drug called clopidogrel (also known as Plavix). Clopidogrel is an antiplatelet drug, which means that it prevents platelets forming blood clots.
- The CYP2C19 enzyme converts clopidogrel to its active form, which is necessary for the drug to function in the body. Polymorphism within this gene is associated with variable ability to metabolize drug, known as the poor metabolizer and extensive metabolizer phenotypes.
- It is important to note that not all individuals with CYP2C19 gene mutations have clopidogrel resistance. These individuals who are at increased risk for developing clopidogrel resistance may or may not have a bad reaction when treated with the drug. In addition to changes in specific genes, many other factors, including sex, age, weight, diet, and other medications, play a role in how the body reacts to clopidogrel.

DISCLAIMER

- This assay screens only the above mentioned alleles in CYP2C19 gene. In cases where none of the variant alleles are detected, a wild type allele (*1) is reported. Kindly note this does not rule out absence of rare CYP2C19 genetic variants not screened in this test. This test covers more than 95 percent of non- functional alleles for the tested population. Drug metabolism may be affected by non-genetic factors. Rare diagnostic errors may occur due to primer-site mutations.
- For questions about this report, or for assistance in locating nearby genetic counselling services, please contact laboratory.
- Although all precautions are taken during DNA tests the currently available data indicate that the technical error rate for all types of DNA analysis is approximately 2%. It is important that all clinicians or persons requesting DNA diagnostic tests are aware of these data before acting upon these results.

REFERENCES:

- Mega, J. L., et al. (2011). "Dosing clopidogrel based on CYP2C19 genotype and the effect on platelet reactivity in patients with stable cardiovascular disease." JAMA306(20): 2221-2228
- Dean, Laura, and Megan Kane. "Clopidogrel therapy and CYP2C19 genotype." *Medical Genetics Summaries [Internet]* (2022).

- #this test is not under NABL scope.

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