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PATIENT NAME	Mrs. ANITHA.M	Barcode No	23824967
Age/Gender	34 Years/F	Reg. No	0012211230096
Referring by		SPP Code	SPL-STS-139
REF. DOCTOR		Collected On	23 Nov 2022
Primary Sample	Whole Blood	Received On	23 Nov 2022
Sample Tested In	Whole Blood EDTA	Reported On	01 Dec 2022

THIO PURINE METHYL TRANSFERASE GENOTYPE STUDY

Test Description	Test Report
TPMT Genotype	TPMT*1/*1

RESULT:

The specimen is NORMAL with respect to TPMT GENOTYPING

INTERPRETATION OF THE RESULT

Individuals with 2 variant alleles have low or no TPMT activity, while those with 1 variant allele have intermediate TPMT activity. Wild-type (TPMT*1) homozygote, on the other hand, have normal enzyme activity.

TPMT Allele	GENETIC VARIANT	dbSNP	PREDICTED ENZYME ACTIVITY
*1	None	----------	NORMAL
*2	c.238G>C	rs1800462	NON-FUNCTIONAL
*3A	c.460G>A and c.719A>G	rs1800460 & rs1142345	NON-FUNCTIONAL
*3B	c.460G>A	rs1800460	NON-FUNCTIONAL
*3C	c.719A>G	rs1142345	NON-FUNCTIONAL

CLINICAL BACK GROUND

Thiopurine drugs (azathioprine, 6-mercaptopurine, and 6-thioguanine) are used to treat patients with leukemia, rheumatic disease, inflammatory bowel disease, or solid organ transplant. These drugs must be metabolized to 6-thioguanine nucleotides (6-TGN) for activity. Thiopurine methyl transferase (TPMT) plays an active role in this drug metabolism pathway and suboptimal activity of TPMT results in impaired drug metabolism causing adverse drug reactions or lack of therapeutic response. Polymorphisms in the TPMT gene results in reduced enzymatic activity. TPMT*2 (238G>C), TPMT*3A (460G>A and 719A>G), TPMT*3B (460G>A), and TPMT*3C (719A>G) accounts for reduced TPMT activity in >95% cases. Patients without a wild-type allele of TPMT gene are at risk of severe haematological toxicities is standard dosages of thiopurine medications are administered to them.

METHODOLOGY

TPMT genotyping analysis is based on PCR followed by automated DNA sequencing using Big Dye Terminator Chemistry on ABI 3500DX Genetic Analyzer to screen four common TPMT variants TPMT*2 (238G>C), TPMT*3A (460G>A and 719A>G), TPMT*3B (460G>A), and TPMT*3C (719A>G).

LIMITATIONS

This assay screens only the above mentioned alleles in TPMT 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 rear TPMT 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.

REFERENCES

- McLeod HL, Siva C. The thiopurine S-methyltransferase gene locus–implications for clinical pharmacogenomics. Pharmacogenomics. 2002; 3:89-98.
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- Yates CR, Krynetski EY, Loennechen T, et al. Molecular diagnosis of thiopurine S-methyltransferase deficiency: genetic basis for azathioprine and mercaptopurine intolerance. Ann Intern Med. 1997; 126:608-614.
- Black AJ, McLeod HL, Capell HA, et al. Thiopurine methyltransferase genotype predicts therapy-limiting severe toxicity from azathioprine. Ann Intern Med. 1998; 129:716-718.
- Kurzawski M, Dziewanowski K, Gawronska-Szklarz B, et al. The impact of thiopurine S-methyltransferase polymorphism on azathioprine-induced myelotoxicity in renal transplant recipients. Ther Drug Monitor. 2005; 27:435-441

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