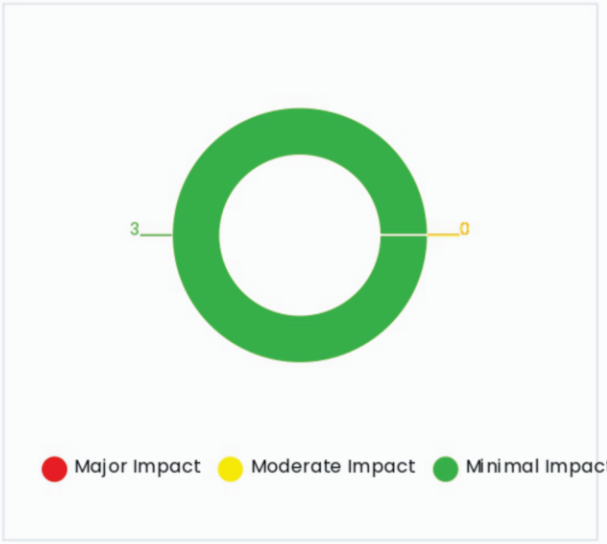
Dr. Vinay Chopra
MD (Pathology & Microbiology)
Chairman & Consultant Pathologist

Dr. Yugam Chopra
MD (Pathology)
CEO & Consultant Pathologist

Patient Sample Details

Name	: YOGITA	**Sex / Age**	: F / 31 Years	**Case ID**	: 40821603696
Ref By	: DR. VINAY CHOPRA	**Test Name**	: TPMT Genotyping	**PT. Loc.**	: KOS DIAGNOSTIC LAB
Date Of Birth (DOB)	:	**Registration Date & Time**	2024-08-25 09:58:30 AM	**Report Date & Time**	: 2024-09-03 10:16:55 PM

Pharmacogenomics Overview



No Action Recommended

Drug	Drug Class	Impact	Interpretation
Mercaptopurine	Antineoplastic Agent	TPMT-Normal Metabolizer,NUDT15-Normal Metabolizer	No Change In Drug Intake
Thioguanine	Antineoplastic Agent	TPMT-Normal Metabolizer,NUDT15-Normal Metabolizer	No Change In Drug Intake
Azathioprine	Immunosuppresant	TPMT-Normal Metabolizer,NUDT15-Normal Metabolizer	No Change In Drug Intake

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Pharmacogenomics Drugs Details

Azathioprine

Disease Category: Inflammation|Transplant Medicine

Gene:		
TPMT,NUDT15	**TPMT*1/*1,NUDT15*1/*1**	**TPMT-Normal Metabolizer,NUDT15-Normal Metabolizer**

TPMT - Lower concentrations of TGN metabolites, higher MeTIMP, this is the 'normal' pattern. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression. NUDT15 - Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression.Start with normal starting dose (e.g., 2-3 mg/kg/day) and adjust doses of azathioprine based on disease-specific guidelines. Allow 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 11302950, 15606506).Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolisers.

Mercaptopurine

Disease Category: Oncology

Gene:		
TPMT,NUDT15	**TPMT*1/*1,NUDT15*1/*1**	**TPMT-Normal Metabolizer,NUDT15-Normal Metabolizer**

TPMT - Normal metabolisers are individuals with two normal function alleles. They have a lower concentration of TGN metabolites, higher MeTIMP, this is the 'normal' pattern. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression. NUDT15 - Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression.Start with normal starting dose (e.g., 75 mg/m2/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 16401827, 11302950).Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolisers.

Thioguanine

Disease Category: Oncology

Gene:		
TPMT,NUDT15	**TPMT*1/*1,NUDT15*1/*1**	**TPMT-Normal Metabolizer,NUDT15-Normal Metabolizer**

TPMT-Normal metabolisers are individual carrying two normal function alleles. Lower concentrations of TGN metabolites, but note that TGN after thioguanine are 5-10X higher than TGN after mercaptopurine or azathioprine. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression. NUDT15 - Normal metabolisers are individuals carrying two functional alleles. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression. Normal starting doses vary by race/ethnicity and treatment regimens. Start with normal starting dose (e.g., 40-60 mg/m2/day) and adjust doses of thioguanine and of other myelosuppressive therapy without any special emphasis on thioguanine. Allow 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 11037857). Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolisers.

Technical Notes

Methodology : Massively Parallel Sequencing (Next Generation Sequencing) Genomic DNA from the submitted

enriched for the complete coding regions and splice site junctions of genes listed below using a custom bait- capture system. Paired End Sequencing was performed with 2x100/2x150 chemistry, on an Illumina platform. Reads were assembled and were aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. Data was filtered and analyzed to identify variants of interest and interpreted in the context of a single most damaging, clinically relevant transcript for the purpose of

Technical Notes

the report, indicated as a part of variant details. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 5-10bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS).

Tools and Databases employed for analysis: Clinvar, OMIM, HGMD, UCSC genome browser, Uniprot, Ensembl, dbSNP, gnomAD, ExAC, Pubmed, Dgap, icgc, Kaviar, various bioinformatics analysis, predictive tools and disease specific databases used as available and appropriate. Such tools/databases would be mentioned wherever used. Interpretations of pharmacogenomic alleles are done through an automated pipeline that takes input NGS data and identifies significant pharmacogenomic alleles in the sample and interpretes the drug responses based on recommendations from published guidelines, like CPIC, RNPgx, CPNDS and DPWG and reviewed databases.

Bioinformatics pipeline version: v14.1.2

Test Limitations

- Testing has been performed assuming that the sample received belongs to the above named individual(s) and any stated relationships between individuals are accepted as true. It is also assumed that consent for the same was provided after pre-test counseling at the point of collection/referral.
- The current results are based on analysis of coding regions (exons) as well as certain intron padding regions on patient's genomic DNA with respect to patient phenotype as defined in the target regions (link available below). However, due to inherent technology limitations, coverage is not uniform across all regions. Hence pathogenic variants present in areas of insufficient coverage as well as those variants which currently do not co-relate with the provided phenotype may not be analyzed/ reported. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity.
- The reported variants have not been Sanger confirmed. Sanger confirmation is recommended for the same.
- The test methodology currently does not detect large deletions/duplications, triplet repeat expansions and epigenetic changes. The test also does not include analysis of predictors for multifactorial, polygenic and/or complex diseases.
- Novel synonymous changes as well as intronic mutations (excluding those affecting invariant splice nucleotides) are not routinely reported.
- Phenotype variability may be due to modifying genetic/non-genetic factors and is not a part of the current analysis.
- This test has not been validated by the FDA, NABL or CAP, and it has been determined by the accrediting bodies that such validation is not required at this time.
- The classification and interpretation of all the variants in this assay reflects the current state of scientific understanding at the time this report was issued. In some instances, the classification and interpretation of such variants may change as new scientific information comes to light. We recommend re- analysis of this report yearly, in order to take advantage of any new scientific data that may become available. Please contact laboratory in case re-analysis of the report is desired. It is the lab's policy to perform re-analysis once on a complimentary basis. However, this re-analysis is performed only when requested.
- The result of this report cannot be extrapolated to a family member of the sampled individual.
- This report does not prescribe any medication or indicate that you need any of the listed drugs. Any change in medication must be done oly under the supervision of a healthcare provider.
- For pediatric samples consent from parents/guardian must be provided.

References

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