Accession ID:	**1603**
Sample Type:	FFPE
Patient's Name:	**XYZ ABC**
Gender/Age:	Male/53

ONCÖCHK

CANCERCHECK100 SOMATIC

Data Uploaded On:	04/02/2025	**Report Generated On:**	04/02/2025

CANCER TYPE:

ascending colon cancer

RESULTS:

List of clinically significant mutations (CSM)

Variants of strong clinical significance:

GENE	VAF	FDA Approved Drugs		
		Responsive	Resistance	Total Clinical Evidence
KRAS (p.Gly12Val)	19.05%		Fruquintinib Panitumumab Tucatinib	
PIK3CA (p.Ile112Profs*15)	17.83%			
PIK3CA (p.Lys111Argfs*34)	17.89%			

Variants of potential clinical significance:

GENE	VAF	FDA Approved Drugs	
		Responsive	Resistance
APC (p.Glu941*)	23.53%		

Technical Information:

Variant	Depth	Genomic location	VAF
KRAS(NM_004985.5);c.35G>T	Total: 609 Alt: 116	chr12:25245350	19.05

Gene summary: KRAS proto-oncogene (KRAS), is a member of the small GTPase superfamily and a key regulator of PI3K and MAPK oncogenic pathways, playing a role in cell proliferation regulation. KRAS mutations including G12D, G12V, G12C, G12A, G12S, G12R, G13D, G13C, and Q61H are identified in a variety of cancers, including non-small cell lung cancer, pancreatic, endometrial, ovarian, biliary and colorecta. Germline KRAS mutations cause cardio-facio-cutaneous (CFC) syndrome and associate with Noonan syndrome (NS)			
PIK3CA(NM_006218.4);c.334_335del	Total: 886 Alt: 158	chr3:179199158	17.83
Gene summary: Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), activates PI3K-AKT-mTOR signaling pathway to promote cell survival, proliferation, growth and motility. PIK3CA is among the most commonly mutated genes in cancer, and PIK3CA activating mutations have been identified in a number of tumor types such as colon cancer, breast cancer, mammary angiosarcoma, endometrial cancer, ovarian cancer, anaplastic thyroid cancer, glioblastoma, and skin cancer. PIK3CA amplification has been observed in esophageal adenocarcinoma and in lung cancer. Somatic mosaicism in PIK3CA, leading to postzygotic activating mutations can cause CLOVE syndrome, megalencephaly-capillary malformation-polymicrogyria (MCAP) syndrome and CLAPO syndrome			
PIK3CA(NM_006218.4);c.332del	Total: 883 Alt: 158	chr3:179199153	17.89
Gene summary: Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), activates PI3K-AKT-mTOR signaling pathway to promote cell survival, proliferation, growth and motility. PIK3CA is among the most commonly mutated genes in cancer, and PIK3CA activating mutations have been identified in a number of tumor types such as colon cancer, breast cancer, mammary angiosarcoma, endometrial cancer, ovarian cancer, anaplastic thyroid cancer, glioblastoma, and skin cancer. PIK3CA amplification has been observed in esophageal adenocarcinoma and in lung cancer. Somatic mosaicism in PIK3CA, leading to postzygotic activating mutations can cause CLOVE syndrome, megalencephaly-capillary malformation-polymicrogyria (MCAP) syndrome and CLAPO syndrome			
APC(NM_000038.6);c.2821G>T	Total: 680 Alt: 160	chr5:112838415	23.53
Gene summary: Adenomatous polyposis coli (APC) is a gene that encodes a tumor suppressor protein that is involved in the β-Catenin/Wnt signaling pathway. APC germline mutations are associated with familial adenomatous polyposis and somatic mutations with colon, endometrial, NSCLC, and breast cancers. APC is altered in many cancers including recurrent somatic mutations R1450*, T1556fs, R876*, R213*, and E1309fs are observed in colon adenocarcinoma, colorectal adenocarcinoma, rectal adenocarcinoma, lung adenocarcinoma, and prostate adenocarcinoma having the greatest prevalence of alterations			

Therapeutic Summary:

Drug	Biomarker	Resistance/Responsive	Level	Clinical Indication
Fruquintinib (Fruzaqla®)	KRAS	**Resistance** | Supports	A	Colorectal cancer
Panitumumab (Vectibix®)	KRAS	**Resistance** | Supports	A	Colorectal Cancer
Tucatinib (Tukysa®)	KRAS	**Resistance** | Supports	A	Colorectal cancer

Recommendations

- Genetic counseling is advised for interpretation on the consequences of the variant(s).
- If results obtained do not match the clinical findings, additional testing should be considered as per referring clinician's recommendation.
- Genetic test results are reported based on the recommendations of Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists
- Sanger validation is recommended for the above listed variants.
- The significance/classification of the variant(s) may change based on genetic testing in the parents and other family members.
- Data revaluation performed upon the up gradation of databases used and results may vary in accordance.

AMP-ASCO-CAP CLASSIFICATION CRITERIA	Methodology
Four-tiered system to categorize somatic sequence variations based on their clinical significance **1. Tier I -** Variants of strong clinical significance. **2. Tier II -** Variants of potential clinical significance. **3. Tier III -** Variants of unknown clinical significance **4. Tier IV -** Benign or likely benign variants	The Genes2Me CancerCheck 100 NGS panel was used for sequencing that screens for 100 clinically relevant genes (coding regions of the genome) for diseases associated with genetic mutations. It covers all major mutations like SNV, InDels & CNV adding up to a target size of 299Kb with hybridization-based target capture technique. After raw data generation, we follow the GATK best practices framework for identification of variants in the sample, starting with raw data quality check using the FastQC followed by BWA read aligner for mapping/aligning to human reference genome GRCh38. After the alignment, GATK Mutect2 algorithm is used for variant calling. Annotation of the variants is performed using open-source available software SnpEff. Further, clinically relevant mutations are annotated using published variants in literature and set of diseases databases – ClinVar, OMIM, COSMIC and HPO. The 1000Genome, gnomAD, dbSNP databases are used for annotation of variants for their minor allele frequency. The dbNSFP database is used for annotation and functional prediction of all potential non-synonymous variants.

Limitations

- Genetic testing is an important part of the diagnostic process however it may not always give a definitive answer. In some cases, a genetic variant may be missed due to the limitations in existing medical knowledge and testing technology. Accurate interpretation of test results is dependent on the availability of biological & medical information (clinical history) of the family, failing to this may leads to incorrect result interpretation and diagnosis.
- Test results are interpreted in the context of clinical findings, available scientific evidences, family history and other laboratory data. The variation(s) which is/are potentially relevant –

Disclaimer

- The interpretation of variants in this report is performed to the best knowledge of the scientific & medical information available at the time of reporting. The classification of variants is based on AMP-ASCO-CAP guidelines.
- As of the inherent technological limitations of the sequencing assay, some of the coding regions can't be properly sequenced, so, variations in these regions may not be identified & interpreted. It is possible that variants not identified by the assay may be associated with the provided phenotypes of the patient.
- It is possible due to insufficient phenotypic

significant related to the patient's provided medical history is/are reported. • Genetic testing is highly accurate but rarely inaccurate results may occur for various reasons like mislabeling of samples, inaccurate clinical/medical family history, rare technical errors or unusual circumstances such as bone marrow transplantation, blood transfusion or the presence of change(s) in such a small percentage of cells that may not be detectable (mosaicism).	information, a gene – variant may be present in data but not selected for analysis and interpretation. • The mutations have not been confirmed by Sanger sequencing. • Genes2Me clarify that the generated report(s) doesn't provide any kind of diagnosis or opinion or recommendation for any disease and its cure in any manner. It is therefore recommended that the patient and/or the guardian(s) of the patient must take the consultation of the clinician or a certified physician or doctor for further course of action. • If the provided material quality and/or quantity not up to the desired level, further procedures will be completed only after getting confirmation from referring clinician/physician only, so, in that case, test(s) result(s) may be misleading or even wrong, therefore, Genes2Me hereby disclaims all liability arising in this connection with the test(s) and report(s). • The analysis pipeline is developed in-house and the performance characteristics of this analysis are determined by Genes2Me only. • This test result should be used as a reference by the healthcare provider for diagnosis and development of treatment plan. • The clinically significant mutations enlisted in this report are provided as a professional service, and are not reviewed or approved by the FDA.

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