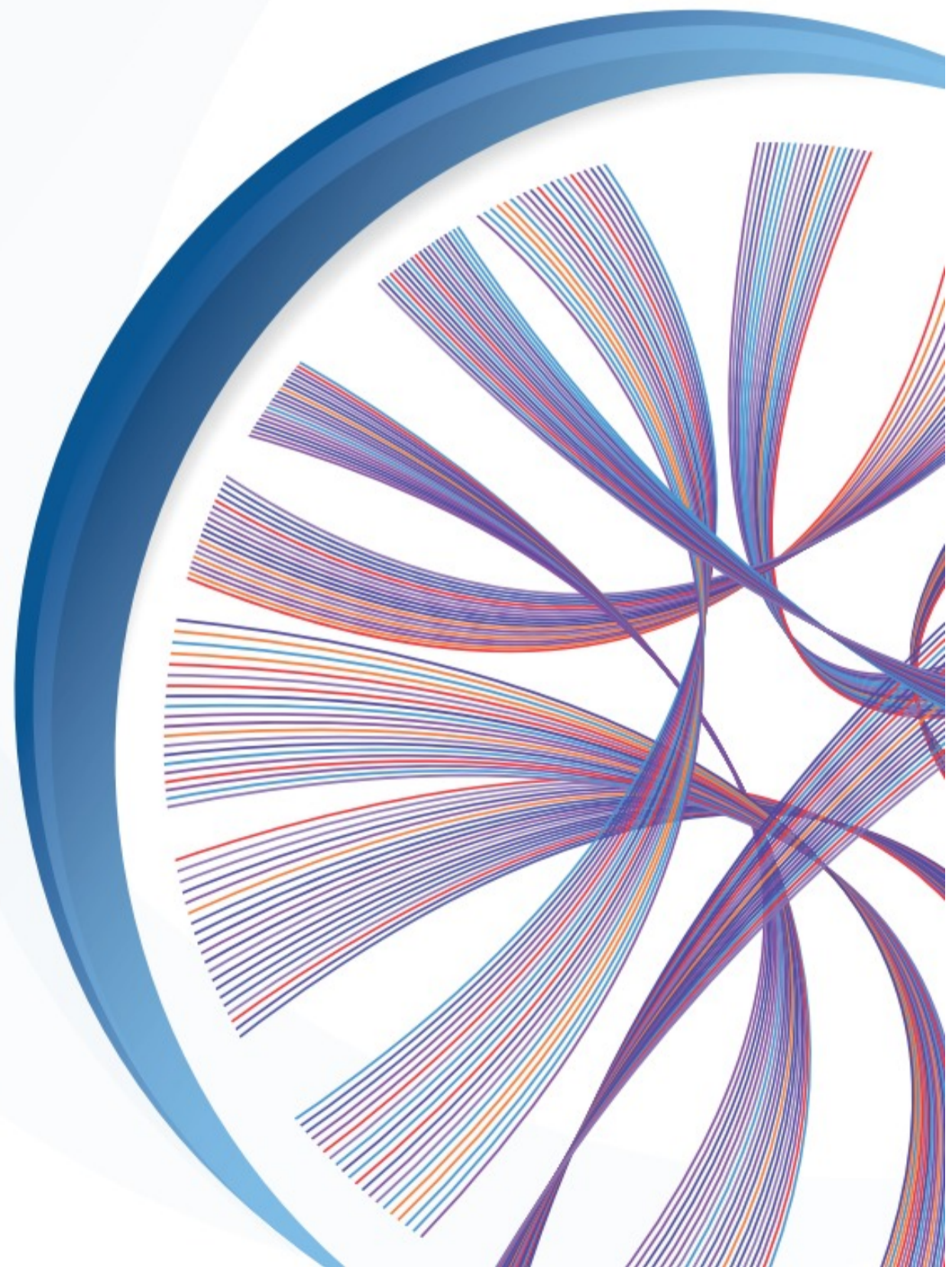


TARGET FIRST

TEST REPORT



SCOPE OF THE TEST

SNVs, InDels, CNAs, Gene Fusions status

CLINICAL INDICATION

Carcinoma of Unknown primary

REPORT DETAILS

Name : SUNIL KUMAR VERMA

Gender : Male

Age/DOB : 48 Years

Reporting Date : 15/03/2023

Sample Source : 1269/22

Tumor content : 40%

Consulting Clinician : Dr. Amit Jain

Hospital : Valentis Cancer Hospital, Mussoorie Mawana Road

RESULTS

GENOMIC FINDINGS FROM TUMOR PROFILING

Genomic
Alteration

Relevant Therapies (in Same Cancer Type)

Relevant Therapies (in Different Cancer)

Clinically relevant genomic alterations associated with therapeutic significance were not detected.

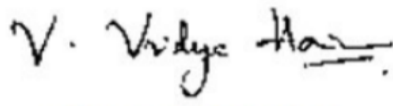
VARIANT DETAILS:

Gene	Variant Location	Variant Consequence	Clinical Significance	Variant Type	Reference
<i>BRCA2</i>	chr13:g.32930675T>A, ENST00000544455, Exon 15	c.7546T>A,p.Ser2516Thr , 53%	VUS	Nonsynonymous SNV	ACMG Guidelines
<i>FGFR3</i>	chr4:g.1806240A>G, ENST00000340107, Exon 9	c.1265A>G,p.Lys422Arg , 48%	VUS	Nonsynonymous SNV	rs762949938, ACMG Guidelines

*NA: Not Applicable

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Vidya H Veldore, PhD
Clinical Director



Vyomesh Javle
TL - Clinical Bioinformatician



Sharanya J
Team Lead - Clinical Reporting

TEST DESCRIPTION

TARGET First is a Next Generation Sequencing based test which identifies genetic alterations in a comprehensive panel of well curated 53 tumor genes which can impact response to approved therapy for a particular cancer type. Some of the alterations detected may have bearing on prognosis and/or therapeutic options and may provide relevant information that allows oncologists/clinicians to consider various lines of targeted treatment for the patient.

GENES EVALUATED

TARGET First detects mutations (SNVs and Short Indels), Copy Number Variations (CNVs), gene fusions and splice variants in the 53 genes :

SNVs/InDels Covered in TARGET First

ABL1	ALK	AR	ATM	BARD1	BRAF	BRCA1	BRCA2	BRIP1	CDK12
CDK4	CDK6	CDKN2A	CHEK1	CHEK2	EGFR	EPCAM	ERBB2	ERBB3	EZH2
FANCL	FGFR3	GAPDH	IDH1	IDH2	JAK2	KIT	KRAS	MAP2K1	MAP2K2
MDM2	MET	MLH1	MLH3	MSH2	MSH6	NRAS	PALB2	PDGFRA	PDGFRB
PIK3CA	PMS1	PMS2	PPP2R2A	RAD51B	RAD51C	RAD51D	RAD54L	RET	ROS1
STK11	TSC1	TSC2							

CNAs Covered in TARGET First

ABL1	AR	ATM	BARD1	BRCA1	BRCA2	BRIP1	CDK12	CDK4	CDK6
CDKN2A	CHEK1	CHEK2	EGFR	EPCAM	ERBB2	ERBB3	EZH2	FANCL	FGFR3
GAPDH	IDH2	JAK2	KIT	MDM2	NRAS	PALB2	PDGFRA	PDGFRB	PPP2R2A
RAD51B	RAD51C	RAD51D	RAD54L	STK11	TSC1	TSC2			

Gene Fusions Covered in TARGET First

ALK	MET	RET	ROS1
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TEST METHODOLOGY

Sample preparation and Library preparation :

DNA isolated from FFPE, or any other fresh tumor tissue source was used to perform targeted gene capture using a custom capture kit. The libraries were sequenced to mean >250X coverage on Illumina sequencing platform.

Bioinformatics Analysis and Reporting :

The sequences obtained are aligned to human reference genome (GRCh37/hg19) and variant analysis was performed using set of Bioinformatics Pipeline. Only non-synonymous and splice site variants found in the panel consisting of specific set of genes were used for clinical interpretation. Silent variations that do not result in any change in amino acid in the coding region are not reported. Clinically relevant mutations were annotated using published variants in literature and a set of databases – ClinVar, COSMIC and dbSNP. Common variants are filtered based on allele frequency in 1000 Genome Phase 3, ExAC, dbSNP, gnomAD, etc. In the absence of a clinically significant reported known variation(s), pathogenicity will be predicted based on in-silico gene prioritization tools: CADD, SIFT, PolyPhen-2, Condel and Mutation taster and prioritized for clinical correlation. The identified pathogenic variant will be correlated with observed phenotypic features of the patient and interpreted according to American College of Medical Genetics (ACMG) guidelines.

Somatic variants are classified into two tiers based on their level of clinical significance in cancer diagnosis, prognosis, and/or therapeutics as per international guidelines: ACMG, ASCO, AMP, CAP, NCCN and ESMO

LIMITATIONS AND DISCLAIMER

- DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of the many aspects used by the healthcare provider to help with a diagnosis and treatment plan.
- We are using the canonical transcript for clinical reporting which is usually the longest coding transcript with strong/multiple supporting evidence. However, in rare cases, clinically relevant variants annotated in alternate complete coding transcripts could also be reported.
- The contents of this test should be carefully assessed by the treating physician and further interpreted along with clinical, histopathological findings, contraindications and guidelines before deciding the course of therapy.
- The chromosomal aberrations like copy number variations and rearrangements may not be reliably detected with this assay and have to be confirmed by alternate method.
- The sensitivity of this assay to detect large deletions/duplications of more than 10 bp or copy number variations (CNV) is 70-75%. The CNVs detected have to be confirmed by alternate method.
- Most recent block is recommended for testing as the mutation profile may change in response to treatment and hence differ at different sampling points.
- TARGT FIRST test has been developed, validated and performed by 4baseCare Genomics Pvt. Ltd and has not been cleared or approved by the FDA.
- The identified pathogenic variant will be correlated with observed phenotypic features of the patient and interpreted according to (ASCO) guidelines.
- Certain genes may not be covered completely, and few mutations could be missed. A negative result cannot rule out the possibility that the tested tumor sample carries mutations not previously associated with cancer and hence not included in the panel.

