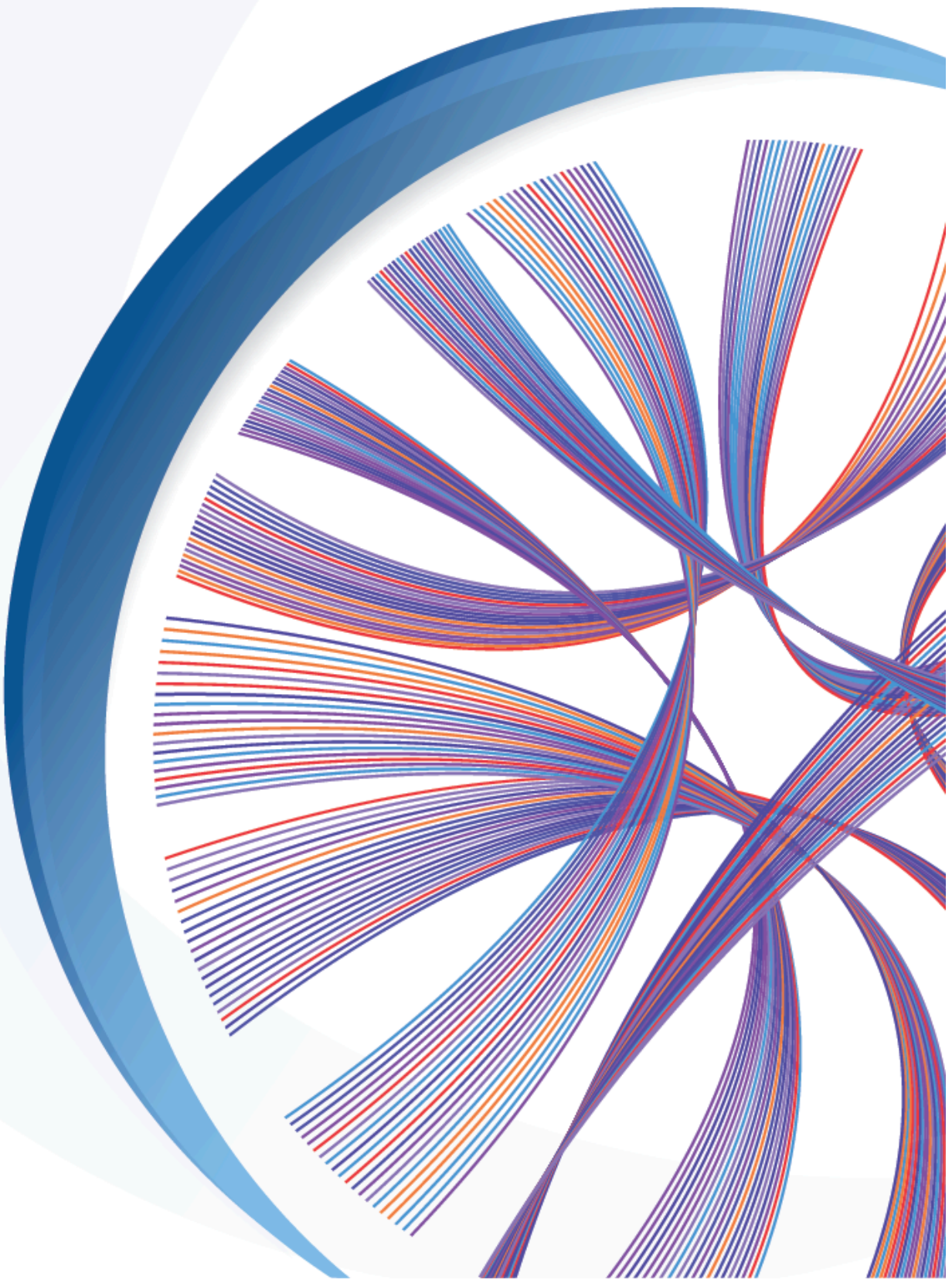
4baseCare
Together, We Beat Cancer

TARGT

First Liquid

TEST REPORT



PATIENT ID	CANCER SITE	SAMPLE ID	REGISTRATION DATE
DB-423-YFWAC	CORPUS UTERI	DB-423-YFWAC-B	23/06/2025

LB-MED-306

INNOVATE LIFE SCIENCES

SCOPE OF THE TEST

SNVs, InDels, CNAs, Gene Fusions status

CLINICAL INDICATION

Endometrium Carcinoma

REPORT DETAILS

Name : SAHIYA HAMID

Gender : Female

Age/DOB : 67 Years

Reporting Date : 02/07/2025

Cancer Celltype : Endometrioid carcinoma

Sample Source : Whole Blood

Consulting Clinician : Dr. Mahendra Perera

Hospital : Aegle Omics (Private) Limited, Sri Lanka

RESULTS

GENOMIC FINDINGS FROM LIQUID BIOPSY PROFILING

Genomic Alteration

CHEK2 Exon 14 (p.Arg517Cys)
Allelic burden: 2%

Relevant Therapies (in Same Cancer Type)

Therapy	*Clinical Relevance*
NA	NA

Relevant Therapies (in Different Cancer)

Therapy	*Clinical Relevance*	*Cancer Type*
Talazoparib with enzalutamide	RESPONSIVE	Prostate cancer
Olaparib	RESPONSIVE	Prostate cancer

**NA: Not Applicable*

PROGNOSTIC BIOMARKERS

Genomic Alteration	Prognostic Significance
Clinically relevant genomic alterations associated with prognostic significance were not detected.	

Amino acids Table:

Ala - A	Arg - R	Asn - N	Asp - D	Cys - C	Glu - E	Gln - Q	Gly - G	His - H	Ile - I
Leu - L	Lys - K	Met - M	Phe - F	Pro - P	Ser - S	Thr - T	Trp - W	Tyr - Y	Val - V

VARIANT DETAILS:

Gene	Variant Location	Variant Consequence	Clinical Significance	Variant Type	Reference
CHEK2	chr22:g.29090061G>A, ENST00000382580, Exon 14	c.1549C>T, p.Arg517Cys, 2%	Likely Pathogenic	Nonsynonymous SNV	rs540635787, VCV000128059.77, ACMG/AMP Guidelines
CHEK2	chr22:g.29121045T>C, ENST00000382580, Exon 5	c.641A>G, p.Asn214Ser, 1%	VUS	Nonsynonymous SNV	rs2146059474, VCV001049312.5, ACMG/AMP Guidelines

**NA: Not Applicable*

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ALTERATIONS WITH CLINICALLY RELEVANT THERAPIES

Gene (Alterations) - Drug association	Summary
• *CHEK2* : Talazoparib with enzalutamide - RESPONSIVE Prostate cancer	The drugs talazoparib with enzalutamide have been approved for homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) (FDA). The approval was based on the clinical study TALAPRO-2 (NCT03395197), a randomized, double-blind, placebo-controlled, multi-cohort trial enrolling 399 patients with HRR gene-mutated mCRPC. A statistically significant improvement in rPFS for talazoparib with enzalutamide compared to placebo with enzalutamide was observed in the HRR gene-mutated population with a median that was not reached vs 13.8 months (HR 0.45; 95% CI: 0.33, 0.61; p<0.0001). In an exploratory analysis by *BRCA* mutation status, the hazard ratio for rPFS in patients with BRCA-mutated mCRPC (n=155) was 0.20 (95% CI: 0.11, 0.36) and, in patients with non-BRCAm HRR gene-mutated mCRPC, was 0.72 (0.49, 1.07).
• *CHEK2* Mutation/Deletion : Olaparib - RESPONSIVE Prostate cancer	The drug olaparib has been approved for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer, who show disease progression after enzalutamide or abiraterone treatment (FDA). The approval was based on the clinical study PROfound (NCT02987543). The study included patients harbouring *BRCA1, BRCA2* and *ATM* mutations (cohort A) and patients harbouring mutations in 12 genes related to HRR pathway (cohort B). A median of 7.4 months progression free survival was recorded based on imaging (HR0.34; 95% CI, 0.25, 0.47; p<0.001) with median overall survival of 18.5 months in cohort A. Olaparib treatment had shown a good response in both cohorts A and B.

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REFERENCES

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* **Note :** This is a system generated report, hence physical signatures are not required.

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TEST DESCRIPTION

TAR**GT** First Liquid is a Next Generation Sequencing based test which identifies genetic alterations in a comprehensive panel of well curated 72 genes which are having an 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

TAR**GT** First Liquid detects mutations (SNVs and Short InDels), Copy Number Variations (CNVs), Gene Fusions and splice variants in the 72 genes:

SNVs, SHORT INDELS and CNVs Covered in TAR**GT** First Liquid

ABL1	*ALK*	*APC*	*AR*	*ATM*	*BARD1*	*BMPR1A*	*BRAF*	*BRCA1*	*BRCA2*
BRIP1	*CDK12*	*CDK4*	*CDK6*	*CDKN2A*	*CHEK1*	*CHEK2*	*CTNNB1*	*EGFR*	*EPCAM*
ERBB2	*ERBB3*	*EZH2*	*FANCL*	*FGFR1*	*FGFR2*	*FGFR3*	*GAPDH*	*IDH1*	*IDH2*
JAK2	*KIT*	*KRAS*	*MAP2K1*	*MAP2K2*	*MDM2*	*MET*	*MLH1*	*MLH3*	*MSH2*
MSH6	*MUTYH*	*NRAS*	*PALB2*	*PDGFRA*	*PDGFRB*	*PIK3CA*	*PMS1*	*PMS2*	*POLD1*
POLE	*POLH*	*PTEN*	*RAD50*	*RAD51*	*RAD51B*	*RAD51C*	*RAD51D*	*RAD54L*	*RB1*
RET	*ROS1*	*SMAD4*	*STK11*	*TP53*	*TSC1*	*TSC2*			

Gene Fusions/Splicing Variations Covered in TAR**GT** First Liquid

ALK	*FGFR2*	*FGFR3*	*MET*	*NRG1*	*NRG2*	*NTRK1*	*NTRK2*	*NTRK3*	*RET*
ROS1									

TEST METHODOLOGY

Sample preparation and Library preparation :

Circulating tumor DNA (ctDNA) isolated from plasma, derived from whole blood was used to perform targeted gene capture using a custom capture kit. The libraries were sequenced to mean >1000X coverage on Element 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 ACMG/AMP guidelines.

Somatic variants are classified into three 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.

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LIMITATIONS AND DISCLAIMER

- TARGT First Liquid test has been developed, validated by 4baseCare Precision Health and has been re-validated and offered for testing at Innovate Life Sciences FZ-LLC, (Dubai). This test 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 AMP guidelines.
- 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 CNVs detected must be confirmed by an alternate method, such as IHC, for further clinical management decision.
- A negative result does not rule out the possibility of mutations in the patient's tumor tissue.
- Our limit of detection for TARGT First Liquid is 1% for SNVs, 5% for InDels and CNV gain ≥ 6. In addition to this, sequencing quality and coverage is dependent on many factors such as homopolymers, GC-rich regions, intrinsic quality of DNA might impact the variant detection.
- 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 that are not previously associated with cancer and hence not included in the panel.
- 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 should be one of the many aspects used by the healthcare provider to help with a diagnosis and treatment plan.
- 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.

End of Report

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