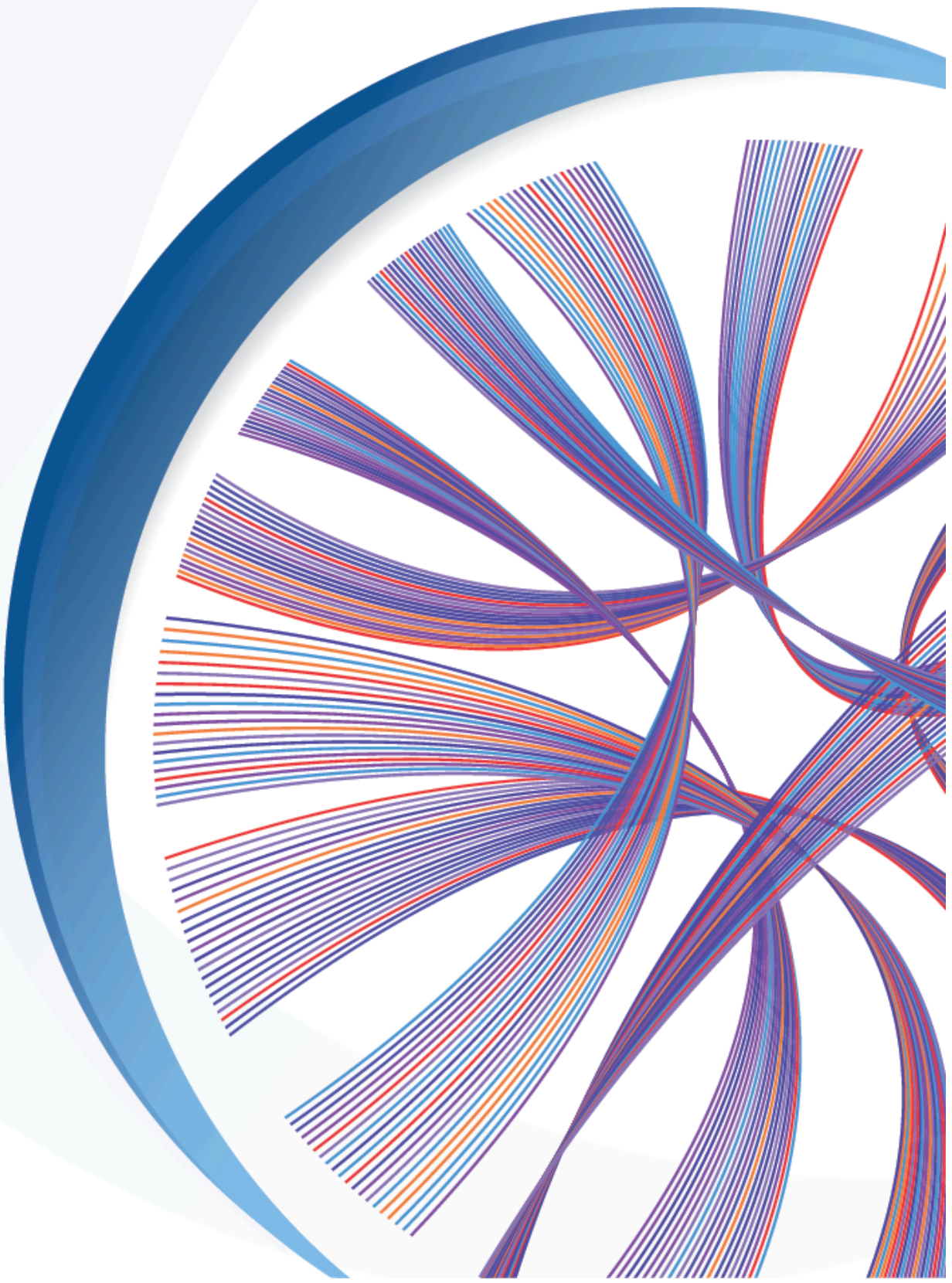
4baseCare
Together, We Beat Cancer

TARGT

First Liquid

TEST REPORT



PATIENT ID	CANCER SITE	SAMPLE ID	REGISTRATION DATE
DB-423-YE1AA	CORPUS UTERI	DB-423-YE1AA-B	27/05/2025

LB-MED-306

SCOPE OF THE TEST

SNVs, InDels, CNAs, Gene Fusions status

CLINICAL INDICATION

Endometrial Endometrioid Adenocarcinoma

REPORT DETAILS

Name : W. SEPALI M. SOYSA

Gender : Female

Age/DOB : 70 Years

Reporting Date : 03/06/2025

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	Relevant Therapies (in Same Cancer Type)		Relevant Therapies (in Different Cancer)		
	Therapy	*Clinical Relevance*	*Therapy*	*Clinical Relevance*	*Cancer Type*
TP53 Exon 5 (p.Arg175His) Allelic burden: 1%	NA	NA	NA	NA	NA

**NA: Not Applicable*

PROGNOSTIC BIOMARKERS

Genomic Alteration	Prognostic Significance
TP53 (p.Arg175His) Allelic burden : 1%	Associated with Poor Prognosis

STATUS OF VARIANTS IN CANCER RELATED BIOMARKERS

Gene	*APC*	*ATM*	*BARD1*	*BRCA1*	*BRCA2*	*BRIP1*	*CDK12*	*CHEK1*
Status	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected

Gene	*CTNNB1*	*EPCAM*	*ERBB2*	*FGFR2*	*KRAS*	*MLH1*	*MSH2*	*MSH6*	*PIK3CA*
Status	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected

Gene	*PMS1*	*PMS2*	*POLE*	*PTEN*	*RAD54L*	*TP53*
Status	Not Detected	Not Detected	Not Detected	Not Detected	Not Detected	**Pathogenic**

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
TP53	chr17:g.7578406C>T, ENST00000269305, Exon 5	c.524G>A, p.Arg175His, 1%	Pathogenic	Nonsynonymous SNV	rs28934578, VCV000012374.75, ACMG/AMP Guidelines
MLH3	chr14:g.75513258G>C, ENST00000355774, Exon 2	c.3101C>G, p.Thr1034Ser, 45%	VUS	Nonsynonymous SNV	rs557921152, VCV001506235.9, ACMG/AMP Guidelines
MET	chr7:g.116340328G>A, ENST00000318493, Exon 2	c.1190G>A, p.Cys397Tyr, 49%	VUS	Nonsynonymous SNV	rs1018999843, VCV001810495.5, ACMG/AMP Guidelines

**NA: Not Applicable*

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ALTERATIONS ASSOCIATED WITH PROGNOSTIC SIGNIFICANCE

Gene (Alterations)	Prognostic Significance	Summary
TP53 (p.Arg175His)	Poor	*TP53* is a tumour suppressor gene which is altered in 39.52% of all cancers. p53 inactivation and mutant p53 expression can grant cells with additive growth and survival advantages, such as increased proliferation, evasion of apoptosis, and chemoresistance. Multiple clinical studies involving cohorts of endometrial cancer patients with p53 mutated tumours suggested a significant association with p53 mutations and poor prognosis (Schultheis AM *et al.*, 2016; Sakuragi *et al.*, 2005; Saffari B *et al.*, 2005). In a study, p53 mutated endometrial cancer patients were associated with worse overall survival (p= 0.035) and higher tumour grade (p<0.0001), as compared to patients with wild type p53 tumours (Schultheis AM *et al.*, 2016). Further, endometrial cancer patients with p53 altered tumours treated with adjuvant radiotherapy had substantially increased survival as compared to patients who did not receive adjuvant therapy (p= 0.035) (Saffari B *et al.*, 2005).

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REFERENCES

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- Nykamp K, et al. Sherloc: a comprehensive refinement of the ACMG-AMP variant classification criteria.doi: 10.1038/gim.2017.37. PMID:28492532
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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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