prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

SAMPLE INFORMATION

Name	-	**Date Sp. Extracted**	
ID/Medical ID	-	**Req. Physician**	-
Date of Birth	-	**Report No**	26xxxxxxGR
Material #1	PLASMA	**Date Received**	-
Material #2	WHOLE PERIPHERAL BLOOD	**Date of Report**	-
Sample #1 ID	-	**Tumor type**	GASTRIC CANCER

primeDX - 1021 Unique Genes (38 Fusions) analyzed

1. Clinically Significant Biomarkers*

Biomarker	Result	Therapies with strong clinical significance		Therapies with potential significance	Therapies with potential resistance
		Approved/ Standard of care therapies (Level A)	Therapies in well powered studies (Level B)	Off label/ Investigational therapies (Level C)	
TP53	Exon 7 p.Y234C VAF: 28.7%	-	-	-	-
KRAS	Copy number gain	-	-	-	-
Microsatellite Instability (MSI)	Stable (MSS)	-	-	-	-
Tumor Mutational Burden (TMB)	6.72 Muts/MB	-	-	-	-
Estimated Tumor Fraction	High (16.3%)	Estimated tumor fraction is 16.3%. A substantial ctDNA signal is present. At this level, detection of tumor-derived variants is generally expected with high confidence for reported variants.			

*Note: Variants' Level of Evidence (LoE) (e.g. A, B, C etc) are based on the Joint consensus recommendation of AMP, ACMG, ASCO and CAP for reporting genetic variants in cancer. For a detailed description of the recommendation please refer to Fig. 1

^ The analysis of selected biomarkers included in the present multigene panel is performed within the scope of accreditation according to ELOT EN ISO 15189:2022 (see «Methodology» section). Accreditation according to ELOT EN ISO 15189:2022 applies exclusively to the analytical determination of the selected biomarkers. Interpretations related to the prediction of therapeutic response are not included in the scope of accreditation.

Germline variants

Gene	Variant	Clinical Significance	Zygosity
No pathogenic/likely pathogenic variant was detected			

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

SAMPLE INFORMATION			
Name	-	**Date Sp. Extracted**	
ID/Medical ID	-	**Req. Physician**	-
Date of Birth	-	**Report No**	26xxxxxxGR
Material #1	PLASMA	**Date Received**	-
Material #2	WHOLE PERIPHERAL BLOOD	**Date of Report**	-
Sample #1 ID	-	**Tumor type**	GASTRIC CANCER

primeDX - 1021 Unique Genes (38 Fusions) analyzed

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

SAMPLE INFORMATION			
Name	-	**Date Sp. Extracted**	
ID/Medical ID	-	**Req. Physician**	-
Date of Birth	-	**Report No**	26xxxxxxGR
Material #1	PLASMA	**Date Received**	-
Material #2	WHOLE PERIPHERAL BLOOD	**Date of Report**	-
Sample #1 ID	-	**Tumor type**	GASTRIC CANCER

primeDX - 1021 Unique Genes (38 Fusions) analyzed

2. Methodology

ctDNA analysis was performed using plasma-extracted cfDNA, in combination with DNA extracted from leukocytes as a control to avoid the detection of false positive results due to clonal hematopoiesis mutations. The MagMAX Cell-Free DNA Isolation Kit (Thermofischer Scientific) and the MagCore Genomic DNA Whole Blood Kit (RBC Bioscience) were used for cfDNA and genomic DNA extraction respectively. A capture based targeted next generation sequencing (NGS) analysis was performed, using the Oncology Multi-Gene Variant Assay (GenePlus) which is a qualitative test that detects variants in 1021 tumor-related genes and gene rearrangements / fusions in 38 genes.

Sequencing was carried out on an MGI sequencing platform (DNBSEQ-T7). The analysis includes the entire exon regions of 312 genes, introns/promoters/fusion breakpoint regions of 38 genes and partial coding exons of 709 genes. The test also reports 30+ immune response biomarkers, including Tumor Mutational Burden (TMB) score and Microsatellite Instability (MSI) status. Sequencing data are analyzed through bioinformatics pipeline for variant calling and interpretation using the Gene+Box data analysis and management system. Alteration- and tumor type-specific therapeutic implications are classified using the OncoKB Levels of Evidence system, which assigns clinical actionability to individual mutational events. For additional details about the OncoKB curation process, please refer to the version-controlled OncoKB Curation Standard Operating Procedure.

Sensitivity: Positive reference standards are tested with the assay, all corresponding mutation sites can be accurately detected, and the positive percent agreement (PPA) for all variants (SNVs, Indels, fusions and CNVs) assessed was 100%.

Specificity: Negative reference standards are tested with the assay, and the negative percent agreement (NPA) of SNVs, Indels, fusions and CNVs was 100%. Limit of Detection (LoD): The limit of detection (LoD) of this assay is listed in the table below. The LoD is based on as low as 30 ng of gDNA input for library preparation.

Variant Type	Limit of Detection
Single nucleotide variations (SNV)	VAF ≥0.3%
Insertions/deletions (Indel)	VAF ≥0.3%
Fusion (or rearrangement)	VAF ≥0.5%

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

SAMPLE INFORMATION			
Name	-	**Date Sp. Extracted**	
ID/Medical ID	-	**Req. Physician**	-
Date of Birth	-	**Report No**	26xxxxxxGR
Material #1	PLASMA	**Date Received**	-
Material #2	WHOLE PERIPHERAL BLOOD	**Date of Report**	-
Sample #1 ID	-	**Tumor type**	GASTRIC CANCER

primeDX - 1021 Unique Genes (38 Fusions) analyzed

Tumor Fraction

TF represents the percentage of tumor-derived DNA circulating in the blood relative to total cell-free DNA. Higher TF generally increases the likelihood of detecting tumor-specific variants, while low TF may indicate limited tumor shedding or early disease. Tumor fraction may be influenced by tumor biology, disease burden, and ongoing treatment, and should be interpreted in the appropriate clinical context alongside.

Plasma cell-free DNA (cfDNA) was analyzed using two complementary approaches for ctDNA assessment: a fragmentomics-based method and a mutation-based method. Fragmentomics-based ctDNA estimation was performed using a deep-learning approach that quantifies ctDNA from the density distribution of cfDNA fragment lengths. This method provides a tumor-naive, sample-level estimate of ctDNA burden that does not rely on the detection of specific genomic variants. Tumor fraction estimation is based on fragmentomic patterns and does not directly measure tumor presence. Results should be interpreted as an estimation of ctDNA burden rather than a definitive measure of tumor load. TF was stratified as low (<1%), intermediate (1–10%), and high (≥10%).

In parallel, mutation-based analysis was performed using a tumor-normal approach to identify high-confidence somatic variants in plasma while minimizing background signal from germline variants and clonal hematopoiesis. The variant allele fraction (VAF) of these somatic variants was then used as an orthogonal estimate of ctDNA tumor fraction. Whenever an eligible somatic variant was identified, Fragmentomics-based TF was used as the primary quantitative estimate, while VAF-based TF served as an orthogonal measure of ctDNA burden and as supportive evidence for overall result interpretation. This approach reflects the broader principle that ctDNA tumor fraction can be inferred from a genome-wide signal when informative, and from somatic variant allele fractions when the genome-wide signal is not informative.

Tumor fraction may help contextualize the confidence of plasma-based genomic profiling. Higher tumor fraction is generally associated with greater confidence in negative liquid biopsy findings, whereas low tumor fraction may indicate a higher risk of false-negative plasma results and may warrant correlation with tissue testing or repeat sampling when clinically appropriate.

Biomarkers within the scope of accreditation (ISO15189:2022)

- AKT1, BRAF, BRCA1, BRCA2, EGFR, ESR1, KRAS, PIK3CA, PTEN (SNV/indel detection by NGS)

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148

A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

SAMPLE INFORMATION			
Name	-	**Date Sp. Extracted**	
ID/Medical ID	-	**Req. Physician**	-
Date of Birth	-	**Report No**	26xxxxxxGR
Material #1	PLASMA	**Date Received**	-
Material #2	WHOLE PERIPHERAL BLOOD	**Date of Report**	-
Sample #1 ID	-	**Tumor type**	GASTRIC CANCER

primeDX - 1021 Unique Genes (38 Fusions) analyzed

Disclaimer

1. This test is mainly used to assist clinical decision-making and the result does not represent clinical decision.
2. The test should be interpreted by combining the actual patient context. The medication information provided only on the basis of genetic test results, and the actual medication should follow the physician's instructions.
3. The clinical trials only present partial relevant clinical recruitment trials. For more comprehensive and updated information, please refer to the website: https://clinicaltrials.gov/.
4. As evidence on variants and drugs evolves, previous classifications may later be modified. The interpretation of a variant is based on current available evidence.
5. Sequence variants were reported using Human Genome Variation Society (HGVS) nomenclature. Classification and interpretation of variants follows guidelines of American College of Medical Genetics and Genomics (ACMG), Association of Molecular Pathology (AMP), American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP).
6. Database and references used: Reference genome (GRCh37), annotation using A Locus Reference Genomic (LRG), database referencing 1000G (phaseIII-ucsc), EXAC (0.3.1), dbSNP (147), PolyPhen2/SIFT (ensdb v73), PhyloP (2013-12-06), Clinvar (2018-8) and Cosmic(V80).

Limitations

1. The test is limited to test genomic variations on DNA level and does not involve RNA level or protein level.
2. Limited cell free tumor DNA (ctDNA) amount could result in false negative results.
3. Germline variants in PMS2 gene with VAF>25% are reported.
4. Scientific data show that not all patients carry genomic variations that are associated with targeted drug, therefore not all subjects can be matched with targeted therapies or clear resistance mechanism.
5. Genetic variation beyond the detection range of this test or some non-gene mutation related factors such as drug interactions may affect the clinical effects of drugs.
6. Fraction of base quality ≥ Q30: The proportion of base quality in sequencing data that reaches or exceeds Q30, indicating that the probability of base recognition accuracy rate exceeds 99.9%.
7. Every molecular test has an internal 0.5-1% chance of failure. This is due to rare molecular events and factors related to the preparation and analysis of the samples.

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

SAMPLE INFORMATION			
Name	-	**Date Sp. Extracted**	
ID/Medical ID	-	**Req. Physician**	-
Date of Birth	-	**Report No**	26xxxxxxGR
Material #1	PLASMA	**Date Received**	-
Material #2	WHOLE PERIPHERAL BLOOD	**Date of Report**	-
Sample #1 ID	-	**Tumor type**	GASTRIC CANCER

primeDX - 1021 Unique Genes (38 Fusions) analyzed

3. Quality Control Results

Quality Control Index		Result	Criterion
Sequencing Quality Assessment	Average effective sequencing depth[1]	1248	≥ 1000
	Fraction of target covered with ≥ 50x[2]	100%	≥99%
	Fraction of base quality ≥ Q30[3]	99%	≥80%
Overall Assessment[4]		PASS	

Note:

1. Average effective sequencing depth: Average sequencing depth on target without duplicated reads.
2. Fraction of target covered with ≥ 50x: The proportion of bases that sequencing depth reach or above 50x on target, this index reflecting the coverage uniformity of sequencing.
3. Fraction of base quality ≥ Q30: The proportion of base quality in sequencing data that reach or above Q30, that is the probability of base recognition accuracy rate exceeds 99.9%.
4. Overall Assessment: The quality control overall assessment results are divided into two levels: "PASS" and "RISK". When the overall quality assessment result is "RISK", 94-96% of coverage was achieved in the genes analysed, hence there is a small range where clinical actionable variations could be undetected.

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name GHANTOUS KAMIL-ANTOINE **Report No** 26016618GR

4. Important biomarkers findings

Gene	Finding (VAF/Copy Number/Germline Mutation)	Detected Range
EGFR	Exon 18	Not detected
	Exon 19	Not detected
	Exon 20 (including T790M)	Not detected
	Exon 21	Not detected
ERBB2 (HER2)	Copy number gain	Not detected
	Mutation	Not detected
ALK	Rearrangement	Not detected
	Mutation	Not detected
ROS1	Rearrangement	Not detected
MET	Copy number gain	Not detected
	Exon 14 skipping	Not detected
RET	Rearrangement	Not detected
	Mutation	Not detected
BRAF	Codon 600 mutation	Not detected
KIT	Exon 9	Not detected
	Exon 11	Not detected
	Exon 13	Not detected
	Exon 17	Not detected
PDGFRA	Exon 12	Not detected
	Exon 18	Not detected
BRCA1	Mutation	Not detected
BRCA2	Mutation	Not detected
KRAS	Codon 12/13/59/61/117/146 mutation	Not detected
	Other mutations except codon 12/13/59/61/117/146	Not detected
NRAS	Codon 12/13/59/61/117/146 mutation	Not detected
	Other mutations except codon 12/13/59/61/117/146	Not detected
PIK3CA	Mutation	Not detected
FGFR2	Rearrangement	Not detected
	Mutation	Not detected
FGFR3	Rearrangement	Not detected
	Mutation	Not detected
NTRK1	Rearrangement	Not detected
NTRK2	Rearrangement	Not detected
NTRK3	Rearrangement	Not detected
IDH1	Mutation	Not detected
PTEN	Mutation	Not detected
AKT1	Mutation	Not detected
ESR1	Mutation	Not detected

Note:

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

1. 'Not detected/-' indicates the corresponding variations were not detected in this tested individual.
2. The genetic variations listed above are covered, but not limited to this list.
3. For a detailed information about listed variants, please refer to the Report Summary and the respective Interpretations sections.

5. Immune Checkpoint inhibitors biomarkers

Biomarker/Variant		Result	Clinical Interpretation
Biomarkers for predicting efficacy			
Tumor mutation burden (TMB)		TMB-L 6.72	-
Microsatellite instability (MSI)		Stable (MSS)	-
Treatment effect - positive correlation			
PD-L1 amplification		Not detected	-
PBRM1 inactivating mutation (Renal clear cell carcinoma)		Not detected	-
MLH1 suspected germline deleterious mutation		Not detected	-
MSH2 suspected germline deleterious mutation		Not detected	-
MSH6 suspected germline deleterious mutation		Not detected	-
PMS2 suspected germline deleterious mutation		Not detected	-
POLE mutation (driver)		Not detected	-
POLD1 mutation (driver)		Not detected	-
Other DNA damage repair (DDR) pathway genes	*ATM* mutation	Not detected	-
	ATR mutation	Not detected	-
	BAP1 mutation	Not detected	-
	BLM mutation	Not detected	-
	BRCA1 mutation	Not detected	-
	BRCA2 mutation	Not detected	-
	BRIP1 mutation	Not detected	-
	CHEK1 mutation	Not detected	-
	CHEK2 mutation	Not detected	-
	ERCC3 mutation	Not detected	-
	ERCC4 mutation	Not detected	-
	ERCC5 mutation	Not detected	-
	FANCA mutation	Not detected	-
	FANCC mutation	Not detected	-
	MRE11A mutation	Not detected	-
	NBN mutation	Not detected	-
	RAD50 mutation	Not detected	-

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

	RAD51 mutation	Not detected	-
	RAD51B mutation	Not detected	-
	RAD51D mutation	Not detected	-
	RAD54L mutation	Not detected	-
TP53 mutation		***p.Y234C (28.7%)***	May increase the benefit rate of PD-1/PD-L1 inhibitors
KRAS mutation		Not detected	-
Treatment effect - negative correlation			
PTEN inactivating mutation		Not detected	-
JAK1 inactivating mutation		Not detected	-
JAK2 inactivating mutation		Not detected	-
B2M inactivating mutation		Not detected	-
EGFR mutation (L858R/EX19del)		Not detected	-
ALK rearrangement		Not detected	-
STK11 inactivating mutation		Not detected	-
KEAP1 inactivating mutation		Not detected	-
11q13 amplification		Not detected	-
MDM2 amplification		Not detected	-
MDM4 amplification		Not detected	-
DNMT3A inactivating mutation		Not detected	-
Indicator affecting prognosis of immune checkpoint inhibitor therapy			
HLA-I Zygosity (At least one of type A, B, C is homozygous)		Not detected	-

Note:

1. Not detected/- indicates the corresponding variation were not detected in this tested individual.
2. The interpretation of the detection results of *PBRM1* inactivating mutations is only applicable to renal clear cell carcinoma.
3. The indicators/gene clinical interpretations listed above are for reference only, and the specific decisions need to refer to professional physician instructions.
4. For a detailed interpretation, showed in Interpretation for biomarker of checkpoint inhibitor.
5. *POLE* and *POLD1* mutations are restricted to currently reported mutations that may lead to hypermutation in tumor, resulting in tumor mutation burden increase.
6. HLA-I results analyzed by the phenotypes of HLA-A, HLA-B and HLA-C loci detected from tumor samples. Due to the lack of control samples, HLA-I typing cannot be accurately analyzed and it is possible that show homozygosity because of the occurrence of HLA-LOH in the tumor tissue.

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

6. Interpretations for targeted therapies

Genetic Variation:	*NM_000546.5* (*TP53*) : c.701A>G (p.Y234C)	VAF*: 28.7%	OncoKB
Therapies:	Under investigation in clinical trials		

Gene information

TP53 encodes the p53 tumor suppressor protein, a transcription factor that responds to cellular stresses, including DNA damage and oncogenic activation, by inducing downstream anti-tumor responses such as DNA repair and apoptosis (PMID: 11099028). p53 levels are kept low in healthy cells due to negative regulation by MDM2/4, Cop1 and Trim24 and constant degradation by the ubiquitin-proteasome system (PMID: 36859359, 36207426). When DNA is damaged, a network of pathways is activated to detect and repair lesions in a cell- and context-specific manner (PMID: 36207426). p53 is rapidly phosphorylated by upstream regulators such as ATM, ATR, and CHL1/2, which results in the accumulation of stable p53 (PMID: 36207426). p53 then binds to specific DNA sequences to direct the expression of a wide variety of genes, including those involved in apoptosis, cell cycle arrest, DNA repair, senescence, stem cell differentiation, autophagy, cellular metabolism, and others (PMID: 27141080, 36859359, 36207426). Oncogenic mutations of TP53 often result in the dysregulation of p53 function, usually due to structural changes in the DNA binding domain (PMID: 36859359). Loss of p53 function can have various outcomes including tumorigenesis, invasion and metastasis, drug resistance, metabolic reprogramming, immune evasion and overall genomic instability (PMID: 36859359). TP53 is the most commonly mutated gene in human cancers, and germline mutations occur in the cancer predisposition syndrome Li-Fraumeni (PMID: 22713868, 21765642). Clinical and preclinical research into drugs that target TP53 is ongoing, notably with MDM2 inhibitors that aim to restore p53 function and are being tested in combination with other cancer therapies (PMID: 36859359, 37818252).

Variant Information

The TP53 Y234C mutation is located in the protein's DNA binding domain. This mutation has been found in ovarian cancer (PMID: 26748848). In vitro studies have demonstrated that this mutation is inactivating, as evidenced by decreased transactivation of p53 target genes, increased cytoplasmic localization and increased apoptosis when treated with an amyloid aggregate TP53 inhibitor in the mutant compared to wildtype, suggesting that this mutation may cause amyloid aggregate formation that inactivates the p53 protein (PMID: 10229196, 16861262, 26748848). The TP53 Y234C mutation is likely pathogenic.

Genetic Variation:	*KRAS*: Copy number gain	VAF*: NA	OncoKB
Therapies:	Under investigation in clinical trials		

Gene information

KRAS is a member of the RAS family of small GTPases, which catalyze the hydrolysis of GTP to GDP. Under physiologic conditions, these RAS proteins cycle between an active (GTP-bound) and an inactive (GDP-bound) state, to activate the MAPK and PI3K oncogenic pathway signaling downstream of Receptor Tyrosine Kinases (RTKs) (PMID: 22189424). The function of RAS enzymes is regulated by guanine nucleotide exchange factors (GEFs), such as SOS, which enable the exchange of GDP to GTP, as well as by GTPase activating proteins, such as NF1, which increase the ability of RAS to hydrolyze GTP. Once activated, RAS mediates the regulation of cellular proliferation and other cellular functions through the activation of distinct intracellular signaling pathways, including the RAF/MEK/ERK and PI3K/AKT/mTOR pathways. Transforming mutations in KRAS are frequently found in pancreatic, colon, endometrial, ovarian and

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

biliary cancers; almost all of these mutations result in constitutive activation of KRAS, thereby promoting cell proliferation (PMID: 21993244, 24651010). KRAS mutations occur primarily in three major hotspots, G12, G13 and Q61, the first two of which occur in the GTP-ase domain and the latter interferes with the ability of NF1 to bind and regulate KRAS (PMID: 22589270, 21993244, 24651010). Other less well-characterized mutations such as A146T/V/P and L19F have also been characterized and found to be activating albeit at lower frequencies (PMID: 20147967, 20432530, 20570890). Germline KRAS mutations are responsible for both Noonan syndrome (NS) and cardio-facio-cutaneous (CFC) syndrome (PMID: 16474405, 16474404, 19467855, 17056636) that are associated with hyperactivated MAPK pathway, distinctive clinical characteristics and a predisposition to cancer (PMID: 19467855, 17704260).

Variant Information

KRAS amplification results in overexpression of the protein. This mutation has been found in germ cell tumors and esophagogastric and ovarian cancer (cBioPortal, Zehir, A et al. Nature Medicine, 2017). In vitro studies have demonstrated that this mutation confers resistance to the tyrosine kinase inhibitor crizotinib, EGFR inhibitors cetuximab or panitumumab, MET inhibitors PHA-665752 or JNJ38877605 and MEK inhibitors AZD6244 or GSK1120212 in patient-derived lung cancer cell line and xenograft models, colorectal cancer cell line models, MET-amplified cell line models and gastric cancer cell line models (PMID: 29808010, 30072474, 23404247, 20841479). Analyses of 475 patients with endometrial cancer demonstrated that KRAS amplification is associated with metastasis (PMID: 23099803). KRAS amplification is likely pathogenic.

*VAF: Variant Allele Frequency

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

7. Interpretation of findings related with chemotherapy drugs

Biomarkers associated with treatment response						
Drug Classes	**Drug name**	**Gene**	**dbSNP**	**Patient's Genotype**	**Patient's Variant-Drug Phenotype Annotation**	**Evidence Level**
Aromatase inhibitors	Letrozole, Anastrozole	*CYP19A1*	rs4646	AA	Associated with better response to treatment	3
	Anastrozole	*ABCB1*	rs2032582	AA	Associated with better response to treatment	3
Cyclophosphamide	Cyclophosphamide	*XRCC1*	rs25487	CT	Associated with poorer response to treatment	4
	Cyclophosphamide	*SOD2*	rs4880	GG	Associated with poorer response to treatment	3
	Cyclophosphamide+Epirubicin	*GSTP1*	rs1695	AG	Associated with better response to treatment	3
Methotrexate	Methotrexate	*ATIC*	rs4673993	TT	Associated with poorer response to treatment	2B
Pemetrexed	Pemetrexed	*MTHFR*	rs1801133	GG	Associated with better response to treatment	3
Platinum-Based Chemotherapy	Platinum compounds	*XRCC1*	rs1799782	GG	Associated with poorer response to treatment	3
	Carboplatin, Cisplatin, Oxaliplatin, Platinum, Platinum compounds	*ERCC1*	rs11615	AG	Associated with poorer response to treatment	3
	Carboplatin, Cisplatin, Oxaliplatin, Platinum, Platinum compounds	*XRCC1*	rs25487	CT	Associated with poorer response to treatment	2B
Taxanes	Paclitaxel+Cisplatin	*TP53*	rs1042522	CG	Associated with poorer response to treatment	3
	Paclitaxel	*ABCB1*	rs2032582	AA	Associated with better response to treatment	3
Vinca alkaloids	Vincristine	*ABCB1*	rs1045642	AA	Associated with poorer response to treatment	3

Biomarkers associated with drug toxicity						
Drug Classes	**Drug name**	**Gene**	**dbSNP**	**Patient's Genotype**	**Patient's Variant-Drug Phenotype Annotation**	**Evidence Level**
5-Fluorouracil (5-Fu), Fluoropyrimidines	5-Fu or Capecitabine	*DPYD*	rs2297595	TT	Associated with decreased risk of drug toxicity	1A
	5-Fu or Capecitabine	*MTHFR*	rs1801133	GG	Associated with decreased risk of drug toxicity	3
	5-Fu+Leucovorin or Tegafur+Leucovorin	*UMPS*	rs1801019	CG	Associated with decreased risk of drug toxicity	3
	Fluoropyrimidine-based therapy	*DPYD*	rs67376798	TT	Associated with decreased risk of drug toxicity	1A
	Fluoropyrimidine-based therapy	*DPYD*	rs55886062	AA	Associated with decreased risk of drug toxicity	1A

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

	Fluoropyrimidine-based therapy	*DPYD*	rs3918290	CC	Associated with decreased risk of drug toxicity	1A
Anthracyclines	Anthracyclines	*CBR3*	rs1056892	AA	Associated with decreased risk of drug toxicity	3
Capecitabine	Capecitabine-Based Chemotherapy	*MTHFR*	rs1801131	TT	Associated with decreased risk of drug toxicity	3
	Capecitabine-Based Chemotherapy	*DPYD*	rs2297595	TT	Associated with decreased risk of drug toxicity	1A
	5-Fu or Capecitabine	*MTHFR*	rs1801133	GG	Associated with decreased risk of drug toxicity	3
	Capecitabine	*DPYD*	rs67376798	TT	Associated with decreased risk of drug toxicity	1A
	Capecitabine	*DPYD*	rs55886062	AA	Associated with decreased risk of drug toxicity	1A
	Capecitabine	*DPYD*	rs3918290	CC	Associated with decreased risk of drug toxicity	1A
Cyclophosphamide	Cyclophosphamide+Epirubicin	*GSTP1*	rs1695	AG	Associated with decreased risk of drug toxicity	3
Gemcitabine	Gemcitabine	*CDA*	rs2072671	AC	Associated with decreased risk of drug toxicity	3
Irinotecan	Irinotecan	*UGT1A1*	rs8175347	6TA/7TA	Associated with moderate risk of drug toxicity	1A
	Irinotecan	*UGT1A1*	rs4148323	GG	Associated with decreased risk of drug toxicity	1B
	Irinotecan	*C8orf34*	rs1517114	CC	Associated with increased risk of drug toxicity	3
Methotrexate	Methotrexate	*MTRR*	rs1801394	AG	Associated with increased risk of drug toxicity	3
	Methotrexate	*ABCB1*	rs1045642	AA	Associated with increased risk of drug toxicity	3
Platinum-Based Chemotherapy	Cisplatin	*XPC*	rs2228001	GT	Associated with increased risk of drug toxicity	3
	Platinum compounds	*GSTP1*	rs1695	AG	Associated with moderate risk of drug toxicity	3
	Cisplatin, Platinum, Platinum compounds	*ERCC1*	rs3212986	AC	Associated with increased risk of drug toxicity	3
	Carboplatin, Cisplatin, Oxaliplatin, Platinum, Platinum compounds	*ERCC1*	rs11615	AG	Associated with increased risk of drug toxicity	3

Note:

1. The level of variant-drug associations evidence is based on PharmGKB website, for more detailed information please see http://www.pharmgkb.org/page/clinAnnLevels.Level 1A: Annotation for a variant-drug combination in a CPIC- or medical society-endorsed pharmacogenomics guideline, or implemented at a PGRN site, or in another major health system;Level 1B: Annotation for a variant-drug combination in which the preponderance of evidence shows an association. The association must be replicated in more than one cohort with significant P-values, and, preferably with a strong effect size;|Level 2A: Annotation for a variant-drug combination that qualifies for level 2B where the variant is within a VIP (Very Important Pharmacogene) as defined by PharmGKB. The variants in level 2A are in known pharmacogenes, so functional significance is more likely;Level 2B: Annotation for a variant-drug combination with moderate evidence of an association. The association must be replicated, but there may be some studies that do not show statistical significance, and/or the effect size may be small;Level 3: Annotation for a variant-drug combination based on a single significant (not yet replicated) study or annotation for a variant-drug combination evaluated in multiple studies but lacking clear evidence of an association;Level 4: Annotation based on a case report, non-significant study, or in vitro, molecular, or functional assay evidence only.
2. The variant-drug correlation relationship derived from multiple independent studies, therefore, the interpretations of the same class of drug for the tested individual may be inconsistent. The final drug instruction needs to combine with the specific clinical situation.

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

8. Other Genomic findings

***Note:**In this section, damaging variants in genes without clinical actionability or without convincing evidence of cancer association are reported.

Genetic Variation	-
Therapies	-

9. Variants of Uncertain Significance (VUS)

The clinical significance of the variants listed in the below table is uncertain at this time. Until the uncertainty is resolved, these variants should not be used in clinical management decisions.

Gene	Variant	Interpretation
SMARCA4	c.3370C>T (p.L1124F)	SMARCA4 (SWI/SNF Related, Matrix Associated, Actin Dependent Regulator Of Chromatin, Subfamily A, Member 4) encodes a member of the SWI/SNF family of proteins that plays a role in transcriptional activation of genes normally repressed by chromatin. Mutations in SMARCA4 have been linked to rhabdoid tumors as well as breast, prostate, lung, pancreas, and colon cancers (PMID: 18437052PMID: 24145903PMID: 19234488). A missense alteration in SMARCA4, p.L1124F, is identified in this case. This variant is of uncertain clinical significance (ACMG & ClinGen classification).

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148
A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

10. Germline variants

Gene	Transcript	Exon	c.HGVS	p.HGVS	Classification
-	-	-	-	-	-

Note:

1. indicates no relevant variations were detected in this test.
2. When detected, pathogenic or likely pathogenic variants are reported. Variants of uncertain significance or variants that are benign or likely benign are not reported.
3. Variant classification interpretation is based on ACMG (American College of Medical Genetics and Genomics) guidelines for the interpretation of germline sequence variants (PMID: 25741868).

11. HLA-I Polymorphism variation

Somatic HLA-I Zygosity

The anti-tumor activity of immune checkpoint inhibitor therapy is related to CD8+ T cells. The recognition of cancer cells by CD8+ T cells is achieved by HLA-I (human leukocyte antigen class I) molecules presenting tumor antigens.

HLA alleles have the characteristics of polymorphism and codominance. HLA-I loci subdivided into HLA-A, HLA-B and HLA-C. When a patient's HLA-I is homozygous at least one locus, this patient is expected to present less and less diverse tumor neoantigens to T cells compared to patients who are heterozygous at all three loci. In two cohorts, patients with heterozygous HLA-I showed longer OS than those with homozygous alleles, cohort1: HR=1.4 (1.02-1.9), P-value=0.036; cohort2: HR=1.31 (1.03- 1.7), P-value=0.028; among 32 patients with heterozygous HLA-I but at least one locus with LOH (loss of heterozygosity), patients with HLA-I LOH have a higher survival risk (P = 0.05, HR = 1.60, 95% CI 1.03-2.43), and these patients mainly with low mutation burden (P = 0.0006, HR = 3.68, 95% CI 1.64-8.23) (PMID: 29217585).

Gene	Test Content	Result
HLA-A	Zygosity	Heterozygosity
HLA-B	Zygosity	Heterozygosity
HLA-C	Zygosity	Heterozygosity

52, Spaton Ave., 15344, Gerakas, Greece, G.E.MI. nr: 0007856001000 | info@genekor.com, www.genekor.com | Tel. (+30) 210 6032138 Fax. (+30) 210 6032148

A company certified with ISO 9001:2015 (Cert. No 041150049) and ISO/IEC 27001:2022(Cert. No 048190009)

-

George Nasioulas, PhD Molecular Biologist, Scientific Director, Medical ID:26025301255

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

12. Clinical Trials to consider

TP53 associated clinical trials

NCT06739395	PHASE2
Title	Precision Medicine Trial Based on Molecular Matching Therapy for Patients With Standard Treatment Exhaustion
Treatment	Olaparib tablet | Temozolomide capsule | Anlotinib | Trametinib tablet | Dabrafenib | Vebreltinib Enteric Capsules | Alpelisib Pill | Sacituzumab Govitecan-Hziy 180 MG | Lenvatinib Capsules | Pazopanib Pill | Palbociclib Pill | Chidamide | PD-1/PD-L1/PD-1&CTLA4 inhibitor | Target Gene
Location	China

NCT06329206	PHASE1
Title	A Phase Ia/Ib Study of GH2616 Tablet in Subjects With Advanced Solid Tumors
Treatment	GH2616 Tablets
Location	China

Press here for a live search of clinical trials for TP53

KRAS associated clinical trials

NCT04116541	PHASE2
Title	A Study Evaluating the Activity of Anti-cancer Treatments Targeting Tumor Molecular Alterations/Characteristics in Advanced / Metastatic Tumors.
Treatment	HDM201 | Ribociclib | Cabozantinib | Alectinib | Regorafenib | Trametinib | Dabrafenib | Avapritinib
Location	France

NCT07223047	PHASE1 | PHASE2
Title	A Study to Evaluate the Safety, Tolerability, and Efficacy of BMS-986523 Alone and in Combination With Anti-Cancer Agents in Participants With Advanced Solid Malignancies
Treatment	BMS-986523 | Gemcitabine | Nab-Paclitaxel | Cetuximab | Pembrolizumab
Location	Canada, Spain, United States

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

NCT06973564	PHASE1 | PHASE2
Title	JAB-23E73 in Adult Participants With Advanced Solid Tumors With KRAS Alteration
Treatment	JAB-23E73 | JAB-23E73 | JAB-23E73
Location	United States

NCT06959615	PHASE1 | PHASE2
Title	A Phase I/IIa Study of JAB-23E73 in Patients With Advanced Solid Tumors Harboring KRAS Gene Alteration
Treatment	JAB-23E73 | JAB-23E73
Location	China

NCT07094113	PHASE1
Title	AMG 410 Alone and in Combination With Other Agents in Participants With KRAS Altered Advanced or Metastatic Solid Tumors
Treatment	AMG 410 | Pembrolizumab | Panitumumab
Location	Australia, Belgium, Canada, China, Denmark, France, Germany, Italy, Japan, Netherlands, South Korea, Spain, United Kingdom, United States

NCT06804824	PHASE1
Title	A First-in-Human (FIH) Study to Evaluate the Safety and Tolerability of VVD-159642 in Participants With Advanced Solid Tumors
Treatment	VVD-159642 | Sotorasib | Trametinib
Location	Australia, United States

NCT07247110	PHASE1
Title	A Clinical Study of MK-4716 in People With Certain Solid Tumors (MK-4716-001)
Treatment	MK-4716 | Pembrolizumab | Cetuximab
Location	Australia, Canada, Chile, Israel, South Korea, Spain, United States

Press here for a live search of clinical trials for KRAS

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

13. Appendix

a. Immune checkpoint inhibitors predictive biomarkers

Tumor Mutation Burden (TMB)

bTMB (blood-based tumor mutational burden) usually refers to the number of somatic nonsynonymous mutations or all mutations per megabase in the gene region examined by whole exome sequencing or targeted sequencing in a tumor peripheral blood sample. bTMB is derived from DNA released into blood circulation by tumor cells (circulating tumor - ctDNA). Tissue TMB (tTMB) is approved as a tumor agnostic biomarker for immunotherapy in patients with metastatic solid tumors. bTMB is positively correlated with tTMB, which can reflect the level of TMB in tumor tissues to some extent. Studies have shown that bTMB is not correlated with the expression of PD-L1 in tumor tissues (PMID: 30082870).

A retrospective analysis confirmed correlation between tTMB and bTMB in patients with NSCLC included in the OAK (NCT02008227, n=850) and Poplar (NCT01903993, n=287) clinical trials of Atezolizumab in second-line treatment for advanced non-small cell lung cancer. High TMB was associated with response to immunotherapy in both trials. A different study successfully correlated blood and tissue TMB results on 2000 NSCLC samples from Geneplus database. The correlation of bTMB with outcomes after front line treatment with Pembrolizumab and Pembrolizumab plus Chemotherapy was also evaluated, at a cutoff of ≥16 mut/Mb, in 66 pts with mNSCLC. Early results suggested that bTMB may predict therapeutic outcomes after first line Pembrolizumab based therapy in mNSCLC. However, the prospective phase III BFAST trial concluded that bTMB at a cut-off of ≥16 mut/Mb was not a predictive biomarker for clinical outcomes with atezolizumab in patients with previously untreated metastatic NSCLC, although the 18-month PFS and OS both numerically favored atezolizumab in this bTMB group (PMID: 35995953).

Evaluation of tissue- and plasma-derived TMB from the CheckMate 848 clinical trial, showed that at the prespecified cutoff of 10 mut/Mb, 15.8% and 20.7% of samples had high tTMB and bTMB, respectively; the positive (PPA), negative and overall percentage agreements between assays were 60%, 88%, and 84%, respectively. TMB correlation (Spearman's r, 0.54; P < 0.0001) and PPA (66%) were improved among 806 (79.3%) sample pairs with plasma maximum somatic allele frequency ≥ 1% (https://doi.org/10.1158/1538-7445.AM2022-2139).

Plasma samples with high bTMB values are highly correspondent with tTMB, whereas bTMB low results may also be the result of low tumor burden at earlier stages of disease as well as poorly shedding tumors (PMID: 35217576). Typically, bTMB reports higher than tTMB, as reported in Drusbosky et al, who analyzed 5610 blood specimens with the 80th percentile bTMB being ≥16 mut/Mb tissue equivalency (PMID: 35274716).

At present, there is no consensus on the application of bTMB in clinical cancer treatment.

Table S1. TMB interpretation and cut-offs

Tumour Type	Immunotherapy agent	Study/Trial	TMB high cut-off	Type of benefit
NSCLC	Anti PD-L1	B1FIRST [1]	**≥16 Muts/Mb**	ORR
NSCLC	Anti PD-L1	BFAST Cohort C [2]	**≥16 Muts/Mb**	-

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

NSCLC	Anti PD-L1	MYSTIC [3]	**≥20 Muts/Mb**	OS
NSCLC	Anti PD-L1	OAK [4]	**≥16 Muts/Mb**	PFS
NSCLC	Anti PD-L1	POPLAR [4]	**≥16 Muts/Mb**	PFS

1.Mok, Tony & Gadgeel, S. & Kim, et al. Blood first line ready screening trial (B-F1RST) and blood first assay screening trial (BFAST) enable clinical development of novel blood-based biomarker assays for tumor mutational burden (TMB) and somatic mutations in 1L advanced or metastatic NSCLC. 2017. Annals of Oncology. 28. 10.1093/annonc/mdx380.084.| **2.** Peters S, et al. Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood-based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial. Nat Med. 2022 Sep;28(9):1831-1839. | **3.** Rizvi NA, et al. MYSTIC Investigators. Durvalumab With or Without Tremelimumab vs Standard Chemotherapy in First-line Treatment of Metastatic Non-Small Cell Lung Cancer: The MYSTIC Phase 3 Randomized Clinical Trial. JAMA Oncol. 2020 May 1;6(5):661-674. doi: 10.1001/jamaoncol.2020.0237. |**4.** Gandara DR, et al. Blood-based tumor mutational burden as a predictor of clinical benefit in non-small-cell lung cancer patients treated with atezolizumab. Nat Med. 2018 Sep;24(9):1441-1448. doi: 10.1038/s41591-018-0134-3.

Microsatellite Instability (MSI)

Microsatellite instability (MSI) is a condition of genetic hypermutability resulting from impaired DNA mismatch repair (MMR) mechanisms. It is characterized by the accumulation of mutations in short repetitive DNA sequences known as microsatellites. MSI-H is found across multiple cancer types, most notably in colorectal, endometrial, gastric, and ovarian cancer. It can arise sporadically or as part of Lynch syndrome, a hereditary condition caused by germline mutations in MMR genes (MLH1, MSH2, MSH6, PMS2).

The results of MSI are divided into three types: MSI-H, which means microsatellites are highly unstable; MSS, which means microsatellites are stable; MSI-U, which means that the sample does not meet the MSI evaluation conditions (tissues or pleural fluid samples may not have passed the MSI indicator calculation quality control due to the low DNA and/or content of tumor cells).

Pembrolizumab has received full FDA approval for adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors((PMID: 35680043, 33264544) — representing the first full approval for an immunotherapy based on a predictive biomarker, regardless of solid tumor type. This approval applies to patients who have progressed after prior treatment and have no satisfactory alternative options. Beyond the tumor-agnostic indication, specific approvals have been granted for tumor types such as endometrial and colorectal cancer.

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

b. Genes Analyzed

312 genes including all exon regions and available for detecting SNV / Indel / CNV									
ABL1	ACVR1B	AKT1	AKT2	AKT3	ALK	APC	AR	ARAF	ARID1A
ARID1B	ARID2	ASXL1	ATM	ATR	ATRX	AURKA	AURKB	AXIN1	AXIN2
AXL	B2M	BAP1	BARD1	BCL2	BCL2L1	BCOR	BLM	BMPR1A	BRAF
BRCA1	BRCA2	BRD4	BRIP1	BTK	CARD11	CASP8	CBFB	CBL	CCND1
CCND2	CCND3	CCNE1	CD274	CDC73	CDH1	CDK12	CDK4	CDK6	CDK8
CDKN1A	CDKN1B	CDKN2A	CDKN2B	CDKN2C	CEBPA	CHEK1	CHEK2	CIC	CREBBP
CRKL	CSF1R	CTCF	CTNNA1	CTNNB1	CUL3	CYLD	DAXX	DDR1	DDR2
DICER1	DNMT3A	DOT1L	EGFR	EIF1AX	EMSY	EP300	EPAS1	EPCAM	EPHA2
EPHA3	EPHA5	EPHB1	EPHB6	ERBB2	ERBB3	ERBB4	ERCC1	ERCC3	ERCC4
ERCC5	ERG	ERRFI1	ESR1	EXT1	EXT2	EZH2	FAM123B	FAM175A	FANCA
FANCC	FANCD2	FANCE	FANCF	FANCG	FANCL	FANCM	FAS	FAT1	FAT2
FBXW7	FGF19	FGF3	FGF4	FGFR1	FGFR2	FGFR3	FGFR4	FH	FLCN
FLT1	FLT3	FLT4	FOXA1	FOXL2	FOXP1	FUBP1	GALNT12	GATA3	GNA11
GNAQ	GNAS	GRIN2A	GRM3	HDAC1	HGF	HNF1A	HOXB13	HRAS	IDH1
IDH2	IFNG	IFNGR1	IGF1R	IKBKE	IKZF1	IL7R	INPP4B	IRF2	IRS2
JAK1	JAK2	JAK3	JUN	KDM5A	KDM5C	KDM6A	KDR	KEAP1	KIT
KRAS	LRP1B	MAF	MAP2K1	MAP2K2	MAP2K4	MAP3K1	MAPK1	MAX	MCL1
MDM2	MDM4	MED12	MEF2B	MEN1	MET	MITF	MLH1	MLH3	MLL
MLL2	MLL3	MPL	MRE11A	MS4A1	MSH2	MSH3	MSH6	MST1R	MTOR
MUTYH	MYC	MYCL1	MYCN	MYD88	NBN	NCOR1	NF1	NF2	NFE2L2
NFKB1A	NKX2-1	NOTCH1	NOTCH2	NOTCH3	NPM1	NRAS	NSD1	NTHL1	NTRK1
NTRK2	NTRK3	PALB2	PARK2	PARP1	PAX5	PBRM1	PCK1	PDCD1	PDCD1LG2
PDGFRA	PDGFRB	PDK1	PIK3CA	PIK3CB	PIK3CG	PIK3R1	PIK3R2	PMS1	PMS2
POLD1	POLE	POT1	PPP2R1A	PRDM1	PRKAR1A	PTCH1	PTCH2	PTEN	PTPN11
PTPRD	RAC1	RAD50	RAD51	RAD51B	RAD51C	RAD51D	RAD52	RAD54L	RAF1
RARA	RB1	RBM10	RECQL	RECQL4	RET	RHOA	RICTOR	RINT1	RNF43
ROS1	RPTOR	RUNX1	SDHA	SDHAF2	SDHB	SDHC	SDHD	SERPINB3	SERPINB4
SETD2	SF3B1	SLX4	SMAD2	SMAD3	SMAD4	SMARCA4	SMARCB1	SMO	SOCS1
SOX2	SOX9	SPOP	SRC	STAG2	STAT3	STK11	SUFU	SYK	TBX3
TCF7L2	TERC	TET2	TGFBR2	TMEM127	TMPRSS2	TNFAIP3	TNFRSF14	TOP1	TOP2A

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

TP53	TSC1	TSC2	TSHR	U2AF1	VEGFA	VHL	WRN	WT1	XPO1
XRCC2	ZMAT3								

38 genes including specific intron, promoter and fusion breakpoint regions and available for detecting gene rearrangement or fusion									
ALK	BCL2L11	BRAF	BRCA1	BRD4	CD74	EGFR	EML4	ERG	ETV6
EZR	FGFR1	FGFR2	FGFR3	KIF5B	KIT	MAML2	MET	MSH2	MYC
MYCL1	NCOA4	NOTCH2	NTRK1	NTRK2	NTRK3	PDGFRA	RAF1	RET	ROS1
RSPO2	SDC4	SLC34A2	TERT	TFE3	TMPRSS2	TPM3	PMS2		

709 genes including partial exon regions and available for detecting SNV / Indel									
ABCA13	ABCB1	ABCC1	ABCC11	ABCC2	ABCG2	ABL2	ACACA	ACIN1	ACTB
ACTG1	ACTG2	ACVR2A	ACVRL1	ADAM29	ADAMTS5	ADCY1	AFF1	AFF2	AFF3
AHNAK	AKAP9	ALB	AMOT	ANGPT1	ANK3	ANKRD11	ANKRD30A	ANKRD30B	APEX1
APOBEC3B	ARAP3	ARFGEF1	ARFGEF2	ARHGAP29	ARHGAP35	ARID4B	ARID5B	ARNT	ASCL4
ASH1L	ASMTL	ASPM	ASTN1	ASXL2	ATIC	ATP11B	ATP12A	ATP1A1	ATP2B3
BAZ2B	BBC3	BBS9	BCAS1	BCL10	BCL11A	BCL11B	BCL2A1	BCL2L11	BCL3
BCL6	BCL9	BCORL1	BCR	BIRC3	BMPR2	BNC2	BPTF	BRD2	BRD3
BRSK1	BRWD1	BTLA	BUB1	C15orf23	C15orf55	C1QA	C1S	C3orf70	C7orf53
C8orf34	CACNA1E	CADM2	CALR	CAMTA1	CASP1	CASQ2	CBLB	CBR1	CBR3
CCDC168	CCNA1	CCNB3	CCT3	CCT5	CCT6B	CD22	CD33	CD5L	CD74
CDA	CDH11	CDH18	CDH23	CDK13	CHD1	CHD1L	CHD4	CHD6	CHD8
CHD9	CHFR	CHI3L1	CHN1	CIITA	CLDN18	CLP1	CLSPN	CLTC	CNOT3
CNOT4	CNTN1	CNTN5	CNTNAP1	CNTNAP5	COL1A1	COL2A1	COL5A1	COL5A2	COL5A3
COPS2	CPS1	CRIPAK	CRLF2	CRNKL1	CRTC1	CSF1	CSF3R	CSMD1	CSMD3
CSNK1A1	CSNK1G3	CTLA4	CTNNA2	CTNND1	CUX1	CXCR4	CYBA	CYP19A1	CYP1A1
CYP1B1	CYP2A13	CYP2C8	CYP2D6	CYP3A4	CYP3A5	DCC	DDX3X	DDX5	DEK
DHX35	DHX9	DIAPH1	DIS3L2	DLC1	DMD	DNAH6	DNAJB1	DNM2	DNMT1
DNMT3B	DOCK2	DOCK7	DPYD	DRGX	DTX1	DUSP22	DYSF	E2F3	EBF1
ECT2L	EED	EEF1A1	EGFL7	EGR3	EIF2AK3	EIF2C3	EIF3A	EIF4A2	EIF4G3
ELAC2	ELF1	ELF3	ELMO1	ELN	EME2	EMID2	EML4	EPC1	EPHA1
EPHA4	EPHA7	EPHB2	EPHB4	EPOR	EPPK1	EPS15	ERBB2IP	ERCC2	ESR2
ETS1	ETV1	ETV5	ETV6	EWSR1	EZR	F8	FAM131B	FAM135B	FAM157B
FAM46C	FAM5C	FAP	FASLG	FAT3	FAT4	FCGR1A	FCGR2A	FCGR2B	FCGR3A

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

FCRL4	FGF10	FGF12	FGF14	FGF23	FGF6	FLG	FLI1	FLNC	FMN2
FN1	FNDC4	FOXA2	FOXO1	FOXO3	FOXQ1	FRMPD4	FUS	FXR1	FYN
FZD1	G3BP1	G3BP2	GAB2	GABRA6	GATA1	GATA2	GFRAL	GIGYF1	GKN2
GLB1L3	GLI1	GLI2	GLI3	GMPS	GNA13	GNG2	GPC3	GPR124	GPS2
GPX1	GRB7	GSK3B	GSTM5	GSTP1	GUSB	H3F3A	H3F3B	H3F3C	HCLS1
HCN1	HDAC4	HDAC9	HECW1	HEY1	HIST1H1C	HIST1H1D	HIST1H1E	HIST1H2AC	HIST1H2AG
HIST1H2AL	HIST1H2AM	HIST1H2BC	HIST1H2BD	HIST1H2BJ	HIST1H2BK	HIST1H2BO	HIST1H3B	HIST1H3C	HIST1H3D
HIST1H3F	HIST1H3G	HIST1H3H	HIST1H3I	HIST1H4I	HIST3H3	HLA-A	HLA-B	HLA-C	HLF
HMCN1	HNF1B	HNRPDL	HOXA11	HOXA13	HOXA3	HOXA9	HOXC13	HOXD11	HOXD13
HSD3B1	HSP90AA1	HSP90AB1	HSPA8	HSPD1	HSPH1	ICK	ICOSLG	ID3	IFITM3
IGF1	IGF2	IGF2R	IGLL5	IKZF2	IKZF3	IL10	IL1RAPL1	IL21R	IL6
IL6ST	IMPG1	ING1	INHBA	INPP4A	INPPL1	INSR	IRF4	IRF6	IRS1
ITGB3	ITK	ITSN1	JARID2	KALRN	KAT6A	KAT6B	KCNJ5	KCNQ2	KDM2B
KEL	KIF5B	KLF4	KLHL6	KLK1	KRTAP5-5	L3MBTL1	LAMA2	LATS1	LATS2
LCP1	LEF1	LGALS8	LIFR	LPHN2	LPP	LRP2	LRP4	LRP5	LRP6
LRRC7	LRRK2	LYN	LZTS1	MACF1	MAD1L1	MAGI2	MAML2	MAML3	MAP3K13
MAPK3	MCC	MCM3	MDC1	MECOM	MEF2C	MGA	MIB1	MIOS	MKL1
MLL4	MLLT3	MMP11	MMP2	MN1	MNDA	MNX1	MSH4	MSN	MSR1
MTHFR	MTRR	MUC5B	MYH11	MYH14	MYH9	MYO3A	MYOD1	NAP1L1	NAV3
NCAM2	NCF2	NCF4	NCK1	NCOA3	NCOA4	NCOR2	NCSTN	NDUFA13	NFATC4
NFE2L3	NKX3-1	NLRC3	NOD1	NOS3	NOTCH4	NQO1	NR1I2	NR2F2	NR4A2
NRG1	NRP2	NRXN1	NTM	NUMA1	NUP107	NUP210	NUP93	NUP98	OBSCN
OGDH	OMD	OPCML	OR11G2	OR2T4	OR4A15	OR4C6	OR5L2	OR6F1	P2RY8
P4HB	PABPC1	PABPC3	PAG1	PAK1	PAK3	PASK	PAX3	PAX7	PC
PCDH18	PCSK6	PCSK7	PDCD11	PDE4DIP	PDGFB	PDILT	PER1	PGR	PHF1
PHF6	PIK3C2A	PIK3C2B	PIK3C2G	PIK3C3	PIM1	PKD1L2	PKHD1	PLAG1	PLCB1
PLCG1	PLCG2	PLK1	PLXNA1	PLXNB2	PNRC1	POLQ	POM121	POM121L12	POU2AF1
PPM1D	PPP1R17	PPP6C	PRDM16	PREX2	PRF1	PRKAA1	PRKCB	PRKCI	PRKDC
PRRX1	PRX	PSG2	PSIP1	PSMB1	PSMB5	PTGS1	PTGS2	PTPN13	PTPN2
PTPRB	PTPRK	PTPRO	PTPRS	PTPRT	PTPRU	RAB35	RAC2	RAD21	RAD54B
RANBP2	RASA1	RASGRP1	RBL1	REL	RELN	RFC1	RGS3	RHEB	RHOH
RHOT1	RIT1	RNASEL	ROBO1	ROBO2	ROBO3	ROCK1	RPGR	RPS6KB1	RPS6KB2
RSPO2	RSPO3	RUNX1T1	RUNX2	RXRA	RYR1	RYR2	SBDS	SCUBE2	SDC4

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

SEC31A	SEMA3A	SEMA3E	SEMA6A	SERPINA7	SETBP1	SETDB1	SF1	SF3A1	SFPQ
SGCZ	SGK1	SH2B3	SH2D1A	SH3PXD2A	SHH	SI	SIN3A	SLC16A1	SLC1A2
SLC22A16	SLC22A18	SLC22A2	SLC22A3	SLC34A2	SLCO1B3	SLIT1	SLIT2	SMARCD1	SMARCE1
SMC1A	SMC1B	SNCAIP	SNTG1	SNX29	SOD2	SOS1	SOX10	SOX17	SPEN
SPRR3	SPSB4	SPTA1	SRD5A2	SRGAP1	SRGAP3	SRSF2	SRSF7	STAG1	STAT1
SUCLG1	SUCLG2	SULT1A1	SUZ12	SVEP1	SYNCRIP	SYNE1	TAF1	TAF15	TAF1L
TAL1	TBL1XR1	TBX15	TBX22	TCEB1	TCF12	TCF3	TCF4	TCL1A	TEC
TENM3	TERT	TET1	TFDP1	TFDP2	TFE3	TGFBR1	THBS2	TJP1	TLE1
TLL2	TLR4	TLX3	TMEM132D	TNFSF11	TNN	TP53BP1	TP63	TP73	TPM3
TPR	TRAF2	TRAF7	TRIM24	TRIM58	TRIO	TRPC5	TRRAP	TSHZ2	TSHZ3
TTF1	TUBA3C	TUBB3	TUSC3	TXNIP	TYMS	TYR	UBE2D2	UBR5	UGT1A1
UMPS	UPF3B	USH2A	USP6	USP8	VEZF1	VIM	VTCN1	WASF3	WDR90
WDTC1	WHSC1	WHSC1L1	WIPF1	WNK1	WNT5A	WSCD2	WWOX	WWP1	WWP2
XIAP	XPC	XRCC1	XRCC3	YAP1	YY1AP1	ZBTB16	ZC3H11A	ZFHX3	ZFP36L1
ZFP36L2	ZFPM2	ZIC3	ZNF217	ZNF384	ZNF521	ZNF638	ZNF750	ZNF804B	

36 HRR genes analyzed									
ATM	ATR	ATRX	BAP1	BARD1	BLM	BRCA1	BRCA2	BRIP1	CDK12
CHEK1	CHEK2	C11orf30	ERCC1	FAM175A	FANCA	FANCC	FANCD2	FANCE	FANCF
FANCG	FANCL	FANCM	MRE11	NBN	PALB2	RAD50	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RECQL	RECQL4	WRN				

64 genes analyzed for germline mutations									
APC	ATM[1]	ATR[1]	ATRX	AXIN2	BAP1[1]	BARD1[1]	BLM[1]	BMPR1A	BRCA1[1,2]
BRCA2[1,2]	BRIP1[1]	CDH1	CDK4	CDKN2A	CHEK2[1,2]	EPCAM[2]	FAM175A[1]	FANCA[1]	FANCL[1]
FANCM[1]	FH	GALNT12	HOXB13	MEN1	MITF	MLH1	MRE11[1]	MSH2[2]	MSH3
MSH6[2]	MUTYH[2]	NBN[1]	NF1	NF2	NTHL1	PALB2[1,2]	PMS2	POLD1	POLE
PTEN	RAD50[1,2]	RAD51B[1]	RAD51C[1,2]	RAD51D[1,2]	RECQL[1]	RECQL4[1]	RET	RNF43	RB1
SDHA	SDHB	SDHC	SDHD	SMAD4	SMARCA4	STK11	TP53[2]	TSC1	TSC2
VHL	WRN[1]	WT1	XRCC2[1]						

Note:

1. Genes of the homologous recombination (HR) complex

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

2. Unless otherwise noted analysis of large rearrangement was performed on the following genes: *BRCA1, BRCA2, CHEK2, EPCAM (Exons 8, 9), MLH1, MSH2, MSH6, MUTYH, PALB2, RAD50 (Exons 1, 2, 4, 10, 14, 21, 23 and 25), RAD51C, RAD51D, and TP53*

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

c. Levels of Evidence for Genomic Biomarkers

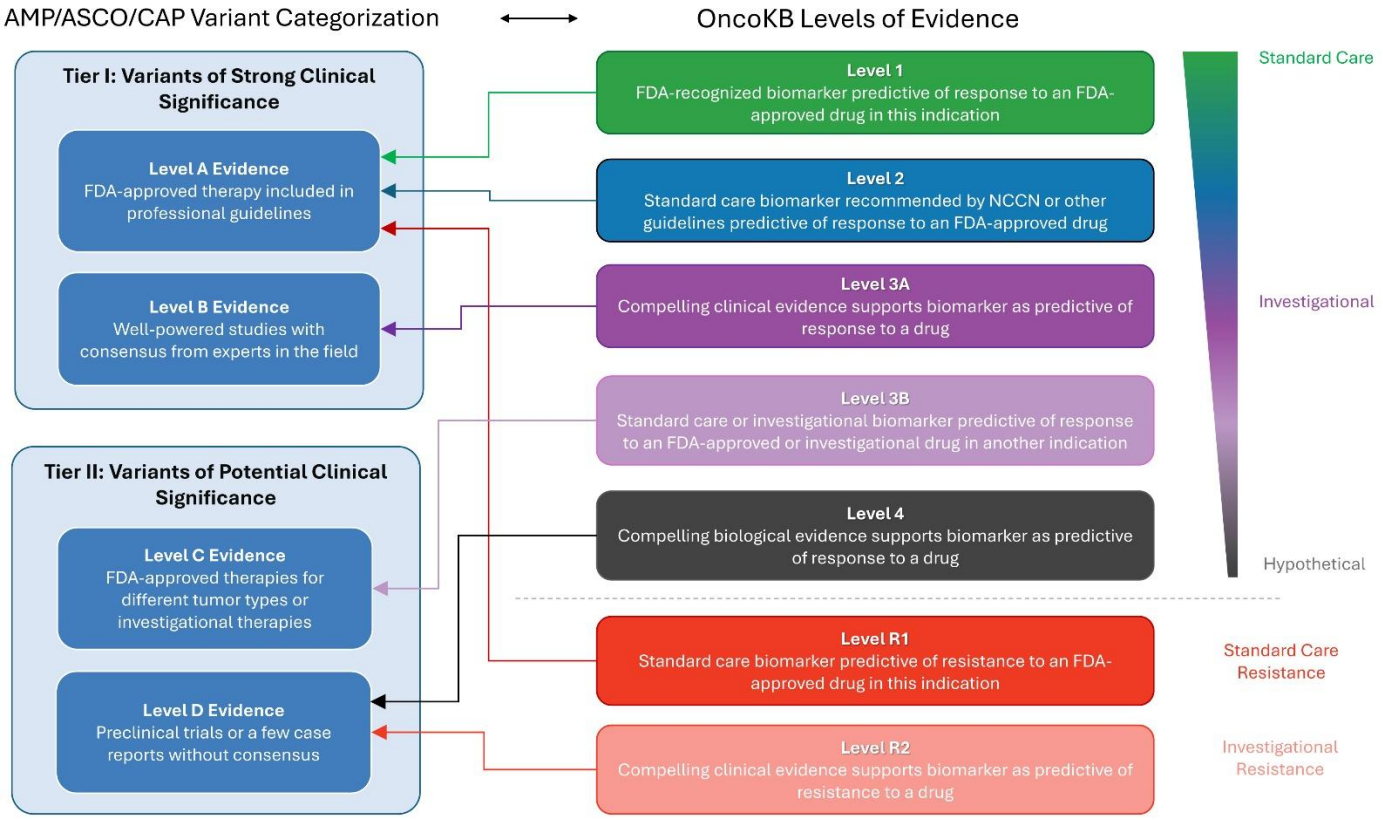

Figure 1. Joint consensus recommendation of AMP, ACMG, ASCO and CAP for reporting genetic variants in cancer. [1-2]

1. Li MM, Datto M, Duncavage EJ, et al. J Mol Diagn. 2017 Jan;19(1):4-23.
2. Leichsenring J, Horak P, Kreutzfeldt S, et al. Int J Cancer. 2019 Dec 1;145(11):2996-3010.

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name - **Report No** 26xxxxxxGR

14. Biomarker findings across all Levels of evidence (A-D)

Biomarker	Result	Therapies with strong clinical significance		Therapies with potential significance		Therapies with potential resistance
		Approved/ Standard of care therapies (Level A)	Therapies in well powered studies (Level B)	Off label/ Investigational therapies (Level C)	Therapies in pre-clinical trials (Level D)	
TP53	Exon 7 c.701A>G (p.Y234C) VAF: 28.7%	-	-	-	-	-
KRAS	Copy number gain	-	-	-	-	-

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

15. References

1. Cepero V, et al. **MET and KRAS gene amplification mediates acquired resistance to MET tyrosine kinase inhibitors.** Cancer Res. 2010; 70:7580-90. doi: 10.1158/0008-5472.CAN-10-0436 (PMID: 20841479)

2. Medina PP and Sanchez-Cespedes M. **Involvement of the chromatin-remodeling factor BRG1/SMARCA4 in human cancer.** Epigenetics. 2008; 3:64-8. doi: 10.4161/epi.3.2.6153 (PMID: 18437052)

3. Ahearn IM, et al. **Regulating the regulator: post-translational modification of RAS.** Nat Rev Mol Cell Biol. 2011; 13:39-51. doi: 10.1038/nrm3255 (PMID: 22189424)

4. Reisman D, et al. **The SWI/SNF complex and cancer.** Oncogene. 2009; 28:1653-68. doi: 10.1038/onc.2009.4 (PMID: 19234488)

5. Smith G, et al. **Activating K-Ras mutations outwith 'hotspot' codons in sporadic colorectal tumours - implications for personalised cancer medicine.** Br J Cancer. 2010; 102:693-703. doi: 10.1038/sj.bjc.6605534 (PMID: 20147967)

6. Birkeland E, et al. **KRAS gene amplification and overexpression but not mutation associates with aggressive and metastatic endometrial cancer.** Br J Cancer. 2012; 107:1997-2004. doi: 10.1038/bjc.2012.477 (PMID: 23099803)

7. Vogelstein B, et al. **Surfing the p53 network.** Nature. 2000; 408:307-10. doi: 10.1038/35042675 (PMID: 11099028)

8. Higgs R. **Screening: A re-evaluation of KRAS mutational 'hotspots'.** Nat Rev Clin Oncol. 2010; 7:242. doi: 10.1038/nrclinonc.2010.54 (PMID: 20432530)

9. Niihori T, et al. **Germline KRAS and BRAF mutations in cardio-facio-cutaneous syndrome.** Nat Genet. 2006; 38:294-6. doi: 10.1038/ng1749 (PMID: 16474404)

10. Valtorta E, et al. **KRAS gene amplification in colorectal cancer and impact on response to EGFR-targeted therapy.** Int J Cancer. 2013; 133:1259-65. doi: 10.1002/ijc.28106 (PMID: 23404247)

11. André T, et al. **Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer.** N Engl J Med. 2020; 383:2207-2218. doi: 10.1056/NEJMoa2017699 (PMID: 33264544)

12. Sturgill EG, et al. **Discordance in Tumor Mutation Burden from Blood and Tissue Affects Association with Response to Immune Checkpoint Inhibition in Real-World Settings.** Oncologist. 2022; 27:175-182. doi: 10.1093/oncolo/oyab064 (PMID: 35274716)

13. Abuetabh Y, et al. **DNA damage response revisited: the p53 family and its regulators provide endless cancer therapy opportunities.** Exp Mol Med. 2022; 54:1658-1669. doi: 10.1038/s12276-022-00863-4 (PMID: 36207426)

14. Lu P and Roberts CW. **The SWI/SNF tumor suppressor complex: Regulation of promoter nucleosomes and beyond.** Nucleus. 2013; 4:374-8. doi: 10.4161/nucl.26654 (PMID: 24145903)

15. Schubbert S, et al. **Germline KRAS mutations cause Noonan syndrome.** Nat Genet. 2006; 38:331-6. doi: 10.1038/ng1748 (PMID: 16474405)

16. Prior IA, et al. **A comprehensive survey of Ras mutations in cancer.** Cancer Res. 2012; 72:2457-67. doi: 10.1158/0008-5472.CAN-11-2612 (PMID: 22589270)

17. Pylayeva-Gupta Y, et al. **RAS oncogenes: weaving a tumorigenic web.** Nat Rev Cancer. 2011; 11:761-74. doi: 10.1038/nrc3106 (PMID: 21993244)

18. Freed-Pastor WA and Prives C. **Mutant p53: one name, many proteins.** Genes Dev. 2012; 26:1268-86. doi: 10.1101/gad.190678.112 (PMID: 22713868)

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

19. Peters S, et al. **Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood-based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial.** Nat Med. 2022; 28:1831-1839. doi: 10.1038/s41591-022-01933-w (PMID: 35995953)

20. Nava C, et al. **Cardio-facio-cutaneous and Noonan syndromes due to mutations in the RAS/MAPK signalling pathway: genotype-phenotype relationships and overlap with Costello syndrome.** J Med Genet. 2007; 44:763-71. doi: 10.1136/jmg.2007.050450 (PMID: 17704260)

21. Alaseem AM. **Advancements in MDM2 inhibition: Clinical and pre-clinical investigations of combination therapeutic regimens.** Saudi Pharm J. 2023; 31:101790. doi: 10.1016/j.jsps.2023.101790 (PMID: 37818252)

22. Gandara DR, et al. **Blood-based tumor mutational burden as a predictor of clinical benefit in non-small-cell lung cancer patients treated with atezolizumab.** Nat Med. 2018; 24:1441-1448. doi: 10.1038/s41591-018-0134-3 (PMID: 30082870)

23. Tidyman WE and Rauen KA. **The RASopathies: developmental syndromes of Ras/MAPK pathway dysregulation.** Curr Opin Genet Dev. 2009; 19:230-6. doi: 10.1016/j.gde.2009.04.001 (PMID: 19467855)

24. Suzuki K and Matsubara H. **Recent advances in p53 research and cancer treatment.** J Biomed Biotechnol. 2011; 2011:978312. doi: 10.1155/2011/978312 (PMID: 21765642)

25. Schuurbiers M, et al. **Biological and technical factors in the assessment of blood-based tumor mutational burden (bTMB) in patients with NSCLC.** J Immunother Cancer. 2022; 10:(unknown pages). doi: 10.1136/jitc-2021-004064 (PMID: 35217576)

26. Janakiraman M, et al. **Genomic and biological characterization of exon 4 KRAS mutations in human cancer.** Cancer Res. 2010; 70:5901-11. doi: 10.1158/0008-5472.CAN-10-0192 (PMID: 20570890)

27. Maio M, et al. **Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study.** Ann Oncol. 2022; 33:929-938. doi: 10.1016/j.annonc.2022.05.519 (PMID: 35680043)

28. Wong GS, et al. **Targeting wild-type KRAS-amplified gastroesophageal cancer through combined MEK and SHP2 inhibition.** Nat Med. 2018; 24:968-977. doi: 10.1038/s41591-018-0022-x (PMID: 29808010)

29. Dearth LR, et al. **Inactive full-length p53 mutants lacking dominant wild-type p53 inhibition highlight loss of heterozygosity as an important aspect of p53 status in human cancers.** Carcinogenesis. 2007; 28:289-98. doi: 10.1093/carcin/bgl132 (PMID: 16861262)

30. Wang H, et al. **Targeting p53 pathways: mechanisms, structures, and advances in therapy.** Signal Transduct Target Ther. 2023; 8:92. doi: 10.1038/s41392-023-01347-1 (PMID: 36859359)

31. Richards S, et al. **Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.** Genet Med. 2015; 17:405-24. doi: 10.1038/gim.2015.30 (PMID: 25741868)

32. Aubrey BJ, et al. **Tumor-Suppressor Functions of the TP53 Pathway.** Cold Spring Harb Perspect Med. 2016; 6:(unknown pages). doi: 10.1101/cshperspect.a026062 (PMID: 27141080)

33. Soragni A, et al. **A Designed Inhibitor of p53 Aggregation Rescues p53 Tumor Suppression in Ovarian Carcinomas.** Cancer Cell. 2016; 29:90-103. doi: 10.1016/j.ccell.2015.12.002 (PMID: 26748848)

34. Bahcall M, et al. **Amplification of Wild-type KRAS Imparts Resistance to Crizotinib in MET Exon 14 Mutant Non-Small Cell Lung Cancer.** Clin Cancer Res. 2018; 24:5963-5976. doi: 10.1158/1078-0432.CCR-18-0876 (PMID: 30072474)

35. Stephen AG, et al. **Dragging ras back in the ring.** Cancer Cell. 2014; 25:272-81. doi: 10.1016/j.ccr.2014.02.017 (PMID: 24651010)

prime DX Liquid
PRECISION INDIVIDUALIZED MEDICINE

Name	-	Report No	26xxxxxxGR

36. Zenker M, et al. **Expansion of the genotypic and phenotypic spectrum in patients with KRAS germline mutations.** J Med Genet. 2007; 44:131-5. doi: 10.1136/jmg.2006.046300 (PMID: 17056636)

37. Smith PD, et al. **Novel p53 mutants selected in BRCA-associated tumours which dissociate transformation suppression from other wild-type p53 functions.** Oncogene. 1999; 18:2451-9. doi: 10.1038/sj.onc.1202565 (PMID: 10229196)