PATIENT

DIAGNOSIS Non-Small Cell Lung Carcinoma
STAGE
NAME John M Doe
DOB 01/23/1950 SEX Male
MRN 123456
ORDER ID Example_report_X1_EPC-ABC-12425
REPORT DATE 03/08/2024

SPECIMEN

SPECIMEN ID 24680
COLLECTION DATE 01/10/2024
RECEIVED DATE 01/12/2024

CLIENT

ORDERING PROVIDER Mary Smith, MD
ORDERING FACILITY United Hospital

Labcorp Plasma Complete Support

For questions or to discuss results:
1-800-781-1259
MedOncSupport@labcorp.com

The Labcorp Plasma Complete test identifies solid tumor-related genomic alterations within 521 genes including amplification in 12 genes, translocations in 12 genes, and microsatellite instability (MSI).

See last page of report for all tested markers

MARKER FINDINGS

See MARKER DETAILS for additional information

Genomic Variants (Positive)	SNV/Indel	**KRAS G12V**
	Translocation	*No positive findings*
	Amplification	*No positive findings*
Signatures	Microsatellite Instability (MSI): MSI Not Detected*	

See APPENDIX: Variants of Unknown Significance

*The MSI Not Detected status is used when ctDNA levels are below the threshold required for MSI-High detection, or the tumor is MSI-Low or MSI-Stable. The MSI Not Detected - Low Coverage status is used when there is low coverage in regions to determine the MSI status.

COMMENTS

Pathologist

No pathologist comments.

Testing

All testing was completed.

THERAPY CONSIDERATIONS

CLINICALLY SIGNIFICANT biomarkers, including genomic variants and signatures, indicate evidence of clinical benefit from or resistance/decreased response to therapy in this patient's tumor type based on FDA approval or professional guidelines. Biomarkers with POTENTIAL CLINICAL SIGNIFICANCE indicate possible clinical benefit based on emerging evidence in this patient's tumor type, including therapies with FDA priority, breakthrough, accelerated, or fast track designation, FDA approval in other tumor types, or as therapy selection markers or drug targets in clinical trials. *(See APPENDIX: Matching & Prioritization of Therapy Considerations)*

CLINICALLY SIGNIFICANT

Clinical Benefit in this Patient's Tumor Type

No marker-directed targeted therapies or immunotherapies with strong evidence of clinical benefit in this patient's tumor type were identified.

Resistance/Decreased Response in this Patient's Tumor Type

			Sources
KRAS G12V	afatinib, dacomitinib, erlotinib, gefitinib, osimertinib	Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.	NCCN

POTENTIAL CLINICAL SIGNIFICANCE

Emerging Clinical Benefit in this Patient's Tumor Type

No marker-directed targeted therapies or immunotherapies with sufficient emerging evidence of clinical benefit in this patient's tumor type were identified.

Clinical Benefit in Other Tumor Types

No marker-directed targeted therapies or immunotherapies with sufficient evidence of clinical benefit in other tumor types were identified.

Clinical Trial Markers for this Patient

KRAS G12V

25 clinical trials

Genomic Variants with No Matched Therapies

No approved therapies or clinical trials identified for this patient

No clinically significant or potentially clinically significant genomic variants without matched therapies or clinical trials were identified.

MARKER DETAILS

MARKER DETAILS provide additional information about genomic variants identified by next generation sequencing (NGS), including single nucleotide variants (SNVs), insertions or deletions (indels), amplifications, translocations, and MSI.

Sequence Alterations

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
KRAS	c.35G>T p.G12V	exon 2	1.1%	Pathogenic	NM_004985.3	Substitution - Missense	MAP kinase signaling

KRAS, KRAS proto-oncogene, GTPase, is a member of the small GTPase superfamily and a key regulator of the MAPK, PI3K/AKT/mTOR pathways (PMID: 23622131) that plays a role in regulation of cell proliferation (PMID: 31988705). KRAS mutations are identified in a wide range of cancers (PMID: 28666118), including colorectal cancer (PMID: 31952666 , PMID: 32241284), non-small cell lung cancer (PMID: 32062493 , PMID: 32244355), and pancreatic cancer (PMID: 32005945). KRAS G12V is a hotspot mutation that lies within a GTP-binding region of the Kras protein (UniProt.org). G12V results in decreased Kras GTPase activity and increased activation of downstream signaling in cell culture, and leads to increased tumor growth in mouse models (PMID: 23455880 , PMID: 26037647 , PMID: 24642870) and is transforming in cell culture (PMID: 29533785).

Amplifications

No clinically significant or potentially clinically significant amplifications were identified for this patient.

Translocations

No clinically significant or potentially clinically significant translocations were identified for this patient.

Microsatellite Instability (MSI)

MSI Not Detected

Microsatellite Instability (MSI) is measured by analyzing potential targeted microsatellites for evidence of instability. MSI is a condition of genetic hypermutability that generates excessive amounts of short insertions/deletions in the genome.

THERAPY DETAILS & CLINICAL TRIALS

THERAPY DETAILS provide select evidence of marker clinical significance for therapeutic response. CLINICAL TRIALS are matched for tested marker results, patient demographics and location within 200 miles of the patient/provider. Clinical trials are prioritized by proximity to the patient/provider and later trial phase. This is not a comprehensive list of all published efficacy data and clinical trials. Information is current as of 09/25/2023. For up to date information regarding available clinical trials, please see www.clinicaltrials.gov

Genomic Variant Clinical Significance

IA FDA-approved or professional guideline-indicated therapies in the tested tumor type

IB Well-powered clinical studies with expert consensus in the tested tumor type

IIC FDA-approved therapies for other tumor types or clinical trial inclusion criteria for the tested tumor type

IID Plausible therapeutic significance with some evidence in the tested tumor type

KRAS G12V

afatinib	NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy. CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.
dacomitinib	NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy. CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.
erlotinib	NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy. CLINICAL SIGNIFICANCE (IA): In a Phase II trial (BATTLE-2), Tarceva (erlotinib) treatment resulted in comparable 8-week disease control rate in KRAS wild-type (36%, 5/14) and KRAS mutated (20%, 1/5) patients with advanced non-small cell lung carcinoma (PMID: 27480147; NCT01248247).
gefitinib	NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy. CLINICAL SIGNIFICANCE (IA): In a clinical study, KRAS codon 12 or 13 mutations were correlated with a lack of response to Iressa (gefitinib) in patients with lung adenocarcinoma (PMID: 15696205).
osimertinib	NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy. CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.
avutometinib	AVUTOMETINIB RO5126766 (VS-6766) is a RAF/MEK inhibitor, which potentially leads to decreased tumor cell growth and inhibition of tumor growth (PMID: 34288272). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT04620330 — A Study of Avutometinib (VS-6766) + Defactinib in Recurrent KRAS G12V, Other KRAS and BRAF Non-Small Cell Lung Cancer — Phase 2 — Columbia, MD
avutometinib + defactinib	AVUTOMETINIB RO5126766 (VS-6766) is a RAF/MEK inhibitor, which potentially leads to decreased tumor cell growth and inhibition of tumor growth (PMID: 34288272). DEFACTINIB Defactinib (VS-6063) inhibits FAK, resulting in decreased downstream signaling, and potentially leading to reduced tumor cell proliferation and survival (PMID: 31739184). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT04620330 — A Study of Avutometinib (VS-6766) + Defactinib in Recurrent KRAS G12V, Other KRAS and BRAF Non-Small Cell Lung Cancer — Phase 2 — Columbia, MD
IMM-1-104	IMM-1-104 IMM-1-104 inhibits MEK1 and MEK2, resulting in decreased downstream ERK1/2 activation and potentially leading to inhibition of tumor growth (Mol Cancer Ther 2021;20(12 Suppl):Abstract nr P252). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT05585320 — A Phase 1/2a Study of IMM-1-104 in Participants With Previously Treated, RAS-Mutant, Advanced or Metastatic Solid Tumors — Phase 1 /Phase 2 — Fairfax, VA

zotatifin	ZOTATIFIN Zotatifin (eFT226) is an eukaryotic initiation factor 4A1 (eIF4A1) inhibitor that promotes binding of eIF4A1 to the 5'-UTR in a sequence selective manner, which leads to repression of mRNA translation, including translation of the receptor tyrosine kinases FGFR1/2 and ERBB2 (HER2), and potentially results in induction of apoptosis and inhibition of tumor growth (Mol Cancer Ther 2019;18(12 Suppl):Abstract nr B133, PMID: 32470302). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04092673	Study of eFT226 in Subjects With Selected Advanced Solid Tumor Malignancies	Phase 1 /Phase 2	Fairfax, VA
BGB3245 + mirdametinib	BGB3245 BGB3245 inhibits RAF dimer formation, which may lead to inhibition of Erk signaling and cell growth (PMID: 29880583). MIRDAMETINIB PD-0325901, a derivative of CI-1040, is a pan-MEK inhibitor, which inhibits activation of MAPK/ERK resulting in decreased tumor cell proliferation (PMID: 18952427, PMID: 32147669). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05580770	Mirdametinib + BGB-3245 in Advanced Solid Tumors	Phase 1 /Phase 2	Philadelphia, PA
DCC-3116; DCC-3116 + binimetinib; DCC-3116 + trametinib	DCC-3116 DCC3116 selectively inhibits ULK1/2, leading to decreased phosphorylation of its substrate ATG13 and inhibition of autophagosome formation, and may lead to inhibition of tumor cell growth (Mol Cancer Ther 2019;18 (12 Suppl):Abstract nr B129). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04892017	A Phase 1/2 Study of DCC-3116 in Patients With MAPK Pathway Mutant Solid Tumors	Phase 1 /Phase 2	Philadelphia, PA
OKI-179 + binimetinib	OKI-179 OKI-179 is a small molecule that inhibits Class I, IIb, and IV histone deacetylases, which may result in reduced tumor growth (PMID: 31235619). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05340621	NAUTILUS: OKI-179 Plus Binimetinib in Patients With Advanced Solid Tumors in the RAS Pathway (Phase 1b) and NRAS-mutated Melanoma (Phase 2)	Phase 1 /Phase 2	Charlottesville, VA
ELI-002	ELI-002 ELI-002 is a peptide-based cancer vaccine consisting of KRAS G12D and G12R peptides with an adjuvant Amph-modified CpG oligonucleotide, which potentially increases antitumor immune response (J Clin Oncol 41, 2023 (suppl 16; abstr 2528)). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05726864	A Study of ELI-002 7P in Subjects With KRAS/NRAS Mutated Solid Tumors	Phase 1 /Phase 2	New York, NY
nivolumab + rigosertib	RIGOSERTIB Rigosertib (ON01910) is a small molecule inhibitor of Plk1, resulting in mitotic cell-cycle arrest and inhibition of tumor growth (PMID: 15766665, PMID: 32442785). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04263090	Rigosertib Plus Nivolumab for KRAS+ NSCLC Patients Who Progressed on First-Line Treatment	Phase 1 /Phase 2	New York, NY
pimasertib + tovorafenib	PIMASERTIB Pimasertib (MSC1936369B) binds to and inhibits MEK1/2, preventing activation of downstream targets and potentially reducing tumor cell proliferation (PMID: 23587417, PMID: 31870556). TOVORAFENIB Tovorafenib (MLN2480) is an inhibitor of pan-Raf kinases, which interrupts RAF/MEK/ERK signal transduction pathways to inhibit tumor cell growth (PMID: 28082416, PMID: 30622172). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04985604	Tovorafenib (DAY101) Monotherapy or in Combination With Other Therapies for Patients With Melanoma and Other Solid Tumors	Phase 1 /Phase 2	Pittsburgh, PA
tovorafenib	TOVORAFENIB Tovorafenib (MLN2480) is an inhibitor of pan-Raf kinases, which interrupts RAF/MEK/ERK signal transduction pathways to inhibit tumor cell growth (PMID: 28082416, PMID: 30622172). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04985604	Tovorafenib (DAY101) Monotherapy or in Combination With Other Therapies for Patients With Melanoma and Other Solid Tumors	Phase 1 /Phase 2	Pittsburgh, PA

MRTX0902	MRTX0902 MRTX0902 inhibits SOS1, blocking interaction with Kras and potentially reducing tumor growth (Cancer Res 2022;82(12_Suppl):Abstract nr ND02). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05578092	A Phase 1/2 Study of MRTX0902 in Solid Tumors With Mutations in the KRAS MAPK Pathway	Phase 1 /Phase 2	Baltimore, MD
nerofe + doxorubicin	NEROFE Nerofe is a 14-amino acid hormone peptide derived from tumor-cells apoptosis factor (TCApF), which potentially induces tumor cell apoptosis, decreases tumor angiogenesis, and enhances antitumor immune response (PMID: 29423221, PMID: 29285362). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05661201	NEROFE and Doxorubicin in KRAS-mutated ST2-positive Solid Tumors	Phase 1	Washington, District of Columbia
BBP-398	BBP-398 BBP-398 is a small molecule SHP2 inhibitor that blocks ERK signaling and potentially reduces tumor cell viability and tumor growth (Mol Cancer Ther 2021;20(12 Suppl):Abstract nr P207). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04528836	First-in-Human Study of the SHP2 Inhibitor BBP-398 in Patients With Advanced Solid Tumors	Phase 1	Fairfax, VA
BDTX-4933	BDTX-4933 BDTX-4933 inhibits BRAF mutations, including class 1, 2 and 3 mutations, and active RAF dimers, which potentially decreases tumor growth (Cancer Res 2023;83(7_Suppl):Abstract nr 3415). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05786924	A Study of BDTX-4933 in Patients With BRAF and Select RAS /MAPK Mutation-Positive Cancers	Phase 1	Fairfax, VA
BMF-219	BMF-219 BMF-219, is an irreversible menin inhibitor, which potentially decreases expression of KRAS, MYC, and BCL2, and reduces tumor growth (Cancer Res 2022;82(12_Suppl):Abstract nr 2665; Blood (2021) 138 (Supplement 1): 4318.). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05631574	Study of Covalent Menin Inhibitor BMF-219 in Adult Patients With KRAS Driven Non-Small Cell Lung Cancer, Pancreatic Cancer, and Colorectal Cancer	Phase 1	Fairfax, VA
HBI-2376	HBI-2376 HBI-2376 inhibits SHP2, potentially leading to decreased tumor cell proliferation and inhibition of tumor growth (Cancer Res 2022;82(12_Suppl):Abstract nr 1041). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05163028	A Dose Escalation Study of SHP2 Inhibitor in Patients With Solid Tumors Harboring KRAS of EGFR Mutations	Phase 1	Fairfax, VA
PRT3645	PRT3645 PRT3645 is a brain-penetrant inhibitor of CDK4 and CDK6, which potentially leads to decreased tumor cell proliferation and tumor growth (Cancer Res (2022) 82 (12_Supplement): 2300). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05538572	A Study of PRT3645 in Participants With Select Advanced or Metastatic Solid Tumors	Phase 1	Fairfax, VA
RMC-6236	RMC-6236 RMC-6236 forms a binary complex with CypA that prevents GTP-bound RAS from interacting with downstream effectors, potentially leading to anti-tumor activity (Cancer Res 2022;82(12_Suppl): Abstract nr 3597). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05379985	Evaluation of RMC-6236 in Subjects With Advanced Solid Tumors Harboring Specific Mutations in KRAS	Phase 1	Fairfax, VA
SPYK04	SPYK04 Limited information is currently available on SPYK04 (Apr 2023). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04511845	A Dose-Escalation Study of SPYK04 in Patients With Locally Advanced or Metastatic Solid Tumors (With Expansion).	Phase 1	Fairfax, VA

nivolumab + BBP-398	BBP-398 BBP-398 is a small molecule SHP2 inhibitor that blocks ERK signaling and potentially reduces tumor cell viability and tumor growth (Mol Cancer Ther 2021;20(12 Suppl):Abstract nr P207). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05375084	SHP2 Inhibitor BBP-398 in Combination With Nivolumab in Patients With Advanced Non-Small Cell Lung Cancer With a KRAS Mutation	Phase 1	Fairfax, VA
JZP815	JZP815 JZP815 is a pan-Raf inhibitor, which potentially inhibits Mapk signaling and tumor growth (Cancer Res 2022; 82(12_Suppl):Abstract nr 2677). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05557045	A Study of JZP815 Oral Capsules in Adult Participants With Advanced or Metastatic Solid Tumors Harboring Mitogen Activated Protein Kinase (MAPK) Pathway Alterations to Investigate the Safety, Dosing, and Antitumor Activity of JZP815	Phase 1	Philadelphia, PA
BGB3245	BGB3245 BGB3245 inhibits RAF dimer formation, which may lead to inhibition of Erk signaling and cell growth (PMID: 29880583). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04249843	Study of Safety, Pharmacokinetics, and Antitumor Activity of BGB-3245 in Participants With Advanced or Refractory Tumors	Phase 1	Charlottesville, VA
ABM-168	ABM-168 ABM-168 inhibits MEK1 and MEK2, potentially resulting in antitumor activity (Cancer Res 2023;83 (7_Suppl):Abstract nr 475). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05831995	Safety and Effectiveness of ABM-168 in Adults With Advanced Solid Tumors.	Phase 1	New Brunswick, NJ
PF-07284892; PF-07284892 + binimetinib	PF-07284892 PF-07284892 is a small molecule inhibitor of SHP2 that may block MAPK signaling and lead to tumor growth inhibition (PMID: 37269335). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04800822	PF-07284892 in Participants With Advanced Solid Tumors	Phase 1	New York, NY
TNO155	TNO155 TNO155 is an inhibitor of PTPN11 (SHP2), which potentially blocks SHP2 signaling, thereby inhibiting activation of the MAPK pathway and subsequent cell growth (NCI Drug Dictionary). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT03114319	Dose Finding Study of TNO155 in Adult Patients With Advanced Solid Tumors	Phase 1	New York, NY
ipilimumab + nivolumab + pooled mutant KRAS-targeted long peptide vaccine	POOLED MUTANT KRAS-TARGETED LONG PEPTIDE VACCINE Pooled mutant KRAS-targeted long peptide vaccine is a mixture of long tumor-specific mutant KRAS peptides, which potentially induces a cytotoxic T-lymphocyte (CTL) response against tumor cells expressing KRAS (NCI Drug Dictionary). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05254184	KRAS-Targeted Vaccine With Nivolumab and Ipilimumab for Patients With NSCLC	Phase 1	Baltimore, MD

APPENDIX Variants of Unknown Significance (VUS)

Genomic variants of unknown significance (VUS) are not well characterized in the scientific literature as of the date of this report.

EGFR G719V	POLD1 S696M	TP53 H168L

APPENDIX About Labcorp Plasma Complete®

INTENDED USE

The Labcorp® Plasma Complete test™ is a next generation sequencing based laboratory developed test for the detection of genomic sequence mutations in 521 clinically actionable or relevant genes including amplifications in 12 genes, translocations in 12 genes, and microsatellite instability (MSI) from plasma-derived cell-free DNA (cfDNA). The test is intended to be used by qualified healthcare professionals in accordance with professional oncology guidelines for patients already diagnosed with advanced stage or metastatic solid tumors. Test results are not prescriptive for the use of any specific therapeutic product.

TEST PRINCIPLE

The Labcorp Plasma Complete test is performed as a laboratory service using cell-free DNA isolated from plasma of peripheral whole blood collected in a Streck cfDNA BCT. Extracted cfDNA is prepared into a hybrid-captured library and sequenced to high depths on an Illumina NovaSeq 6000 instrument. The median total coverage of passing validation samples was 16,369, and average de-duplicated error-corrected coverage was 1,846. Data analysis utilizes proprietary PGDx software that performs alignment, variant calling, and filtering to determine sequence mutations, amplifications, translocations, and MSI status. Variant calls are then clinically annotated and summarized in a clinical report generated through GenomOncology Pathology workbench.

SEQUENCE MUTATIONS

DNA sequencing of the coding regions of 521 genes is performed to detect single nucleotide variants (SNVs) and insertions and deletions (indels) up to 42 bp. Select variants with FDA or guideline-indicated therapies are detected at a minimum of 0.1% variant allele frequency (VAF). Other variants are detected at a minimum of 0.3% or 0.5% VAF depending on their prevalence in COSMIC. Non-coding and synonymous variants are excluded from reporting except for select positions in MET and splice site variants within 2bp of an exon boundary. Common germline alterations present in dbSNP, ExAC, and gnomAD are excluded. Additionally, variants that are not in guidelines and have < 25 hits in COSMIC are excluded if they have ≥ 40% VAF.

AMPLIFICATIONS

DNA sequencing is performed to detect and report amplifications in 12 genes: CCND1, CD274, CDK4, EGFR, ERBB2, FGF19, FGF3, FGF4, FGFR1, MDM2, MET, and MYC. Amplifications are reported if detected fold change is ≥ 1.60.

TRANSLOCATIONS

DNA sequencing is performed to detect translocations in 12 genes: ALK, BRAF, ETV6, EWSR1, FGFR2, FGFR3, NTRK1, NTRK2, NTRK3, RET, ROS1, and TMPRSS2. Translocation calling uses unique reads to score variants, with a minimum number of 2 or 7 unique candidate reads required for reporting. This assay does not detect translocation orientation. Consider additional testing (including RNA testing) to confirm translocation orientation.

MICROSATELLITE INSTABILITY (MSI)

Microsatellite instability (MSI) status is determined by analyzing microsatellite sites for evidence of instability. The proportion of unstable MSI tracts is calculated to inform the reported sample-level MSI score. 3 MSI statuses are possible. 'MSI-High' is defined as > 20% unstable tracts. If MSI-High is not detected, the report will read 'MSI Not Detected.' If MSI-High is not detected due to low coverage in regions used to determine MSI status, the report will read 'MSI Not Detected Low Coverage.'

MARKER CLINICAL SIGNIFICANCE

Labcorp Plasma Complete reported genomic variants are matched to therapies and clinical trials relative to the tested tumor type. Therapy and clinical trial associations for genomic variants are reported as clinically significant or potentially clinically significant in accordance with recommendations described in Li MM, et al., Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagnostics. 2017;19(1):4-23. Genomic variants with potential clinical significance but no therapy considerations as of report date are identified for the tested patient.

REPORTED VARIANTS WITH HIGH VAF

The Labcorp Plasma Complete test is designed to detect somatic variants. The assay filters common germline variants and variants that are likely germline based on variant allele frequency (VAF), except for pathogenic or likely pathogenic variants in select genes, variants in guidelines, and alterations frequently in COSMIC. Reported alterations on page 1 that have a VAF > 40% are listed in the comments section for informational purposes.

REGIONS OF LOW COVERAGE

The Labcorp Plasma Complete test reports detected variants that meet quality control metrics. Negative variant status is not reported. However, if a variant is not detected in select actionable and hotspot regions (n = 29), the region is assessed for low coverage. Assessed regions that do not meet coverage thresholds are listed in the comments section for informational purposes. This section will not appear if all assessed regions meet coverage requirements. Positions with a detected variant are not assessed for low coverage.

MATCHING & PRIORITIZATION OF THERAPY CONSIDERATIONS

Genomic variants from Labcorp Plasma Complete are matched to therapies based on the tested patient's tumor type, FDA regulatory approval status, National Comprehensive Cancer Center (NCCN) professional guideline indications, published emerging efficacy data to support unmet clinical need, including FDA breakthrough and fast track designations (see https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review), potential expanded access/compassionate use (https://www.fda.gov/news-events/public-health-focus/expanded-access), and other peer-reviewed human clinical studies. Therapy Considerations are prioritized as follows: Markers associated with clinical benefit or resistance/decreased response in the patient's tumor type, ordered by approval status and variant clinical significance (if applicable); markers associated with clinical benefit in other tumor types (ordered alphabetically by marker and ranked by variant clinical significance, if applicable); and markers associated with clinical trials (ordered by proximity to the patient and later trial phase). Genomic variants with potential clinical significance but no therapy considerations identified on the report date, are also provided.

PERFORMANCE CHARACTERISTICS

Analytical Sensitivity

Variant Category	Observed Minimum LoD*
SNVs	0.38% VAF**
Indels	0.43% VAF**
Amplifications	1.63 fold
Translocations	0.35% FRF***
MSI	0.11% VAF** of Driver Variant

*LoD (Limit of Detection) calculated for 95% statistical confidence

** VAF (Variant Allele Frequency)

*** FRF (Fusion Read Fraction)

Analytical Specificity

Variant Type	Specificity
SNVs	> 99.99%
Indels	100%
Amplifications	100%
Translocations	100%
MSI	100%

Accuracy

Performance	Observed PPA*	Observed NPA**
SNVs	97.4%	> 99.99%
Indels	91.6%	> 99.99%
Amplifications	100%	99.94%
Translocations	86.4%	100%
MSI	100%	100%

*PPA (Positive Percent Agreement)

**NPA (Negative Percent Agreement)

LIMITATIONS OF PROCEDURE

Labcorp Plasma Complete results may be limited by insufficient coverage in specific regions of the genome, inability to distinguish highly related human sequences, or other technical limitations. A negativeresult does not rule out the presence of an alteration and may be attributed to low levels of circulating tumor DNA (ctDNA) below the limit of detection of the assay, which has not been validated to report wild-type results. Alterations reported may include somatic (not inherited) or germline (inherited) alterations. The assay filters common germline and high variant allele frequency (VAF) variants, except for pathogenic or likely pathogenic variants in select genes, variants in guidelines, and alterations frequently in COSMIC. The test is not intended to replace germline testing or to provide information about cancer predisposition. Genomic findings from cfDNA may originate from ctDNA fragments, germline alterations, or non-tumor somatic alterations, such as clonal hematopoiesis (CH).

DISCLAIMER

This test was developed, and its performance characteristics were determined by Labcorp. It has not been cleared or approved by the Food and Drug Administration.

The selection of any, all, or none of the matched therapies reported by Labcorp Plasma Complete resides solely with the treating physician and should not be solely based on the Labcorp Plasma Complete report. Decisions about patient care and treatment must be based on the independent medical judgement of the treating physician, accounting for all information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the community standard of care. While this report is believed to be accurate and complete as of the date issued, Personal Genome Diagnostics Inc. is not responsible for updating the report to incorporate newly obtained information or new interpretations of the assay results contained in the report.

APPENDIX All Markers Assayed by Labcorp Plasma Complete

DNA-Sequencing of 521 genes for the detection of substitutions, indels, and MSI

ABL1	BCL6	CDKN2C	EP400	FGF23	H1-2	KEAP1	MSH6	PBRM1	PTPRT	SHLD1	TLR9
ABL2	BCOR	CEBPA	EPAS1	FGF3	H3-3A	KEL	MST1R	PDCD1	RAC1	SHLD2	TMPRSS2
ABRAXAS1	BCORL1	CHEK1	EPCAM	FGF4	H3-5	KIT	MTAP	PDCD1LG2	RAD21	SLFN11	TNFAIP3
ACVR1	BCR	CHEK2	EPHA2	FGF6	H3C2	KLF4	MTOR	PDGFRA	RAD50	SLX4	TNFRSF14
ACVR1B	BIRC3	CIC	EPHA3	FGFR1	HDAC1	KMT2A	MUTYH	PDGFRB	RAD51	SMAD2	TOP1
ACVR2A	BIRC5	CREBBP	EPHA5	FGFR2	HDAC2	KMT2B	MYB	PDK1	RAD51B	SMAD3	TOP2A
ADGRA2	BLM	CRKL	EPHB1	FGFR3	HDAC6	KMT2C	MYC	PDPK1	RAD51C	SMAD4	TP53
ADORA2A	BMP1	CRLF2	EPHB4	FGFR4	HGF	KMT2D	MYCL	PGR	RAD51D	SMARCA4	TP53BP1
AHCTF1	BMPR1A	CRTC1	ERBB2	FH	HLA-A	KRAS	MYCN	PHF6	RAD52	SMARCB1	TP63
AKT1	BRAF	CSF1	ERBB3	FLCN	HLA-B	LATS1	MYD88	PHOX2B	RAD54L	SMC3	TRAF3
AKT2	BRCA1	CSF1R	ERBB4	FLI1	HLA-C	LATS2	MYOD1	PIK3C2B	RAF1	SMO	TSC1
AKT3	BRCA2	CSF2	ERCC1	FLT1	HNF1A	LRP1B	NBEA	PIK3C2G	RARA	SOCS1	TSC2
ALB	BRD4	CSF3R	ERCC2	FLT3	HOXB13	LTK	NBN	PIK3C3	RASA1	SOX10	TSHR
ALK	BRD7	CTC1	ERCC3	FLT4	HRAS	LYN	NCOA3	PIK3CA	RB1	SOX17	TYRO3
ALMS1	BRIP1	CTCF	ERCC4	FOXA1	HSP90AA1	LZTR1	NCOR1	PIK3CB	RBM10	SOX2	U2AF1
ALOX12B	BTG1	CTLA4	ERCC5	FOXL2	HUWE1	MAD2L2	NF1	PIK3CD	RECQL4	SOX9	UBE2T
AMER1	BTG2	CTNNA1	ERCC6	FOXO1	ID3	MAF	NF2	PIK3CG	REL	SPOP	VEGFA
APC	BTK	CTNNB1	ERCC8	FOXP1	IDH1	MALT1	NFE2L2	PIK3R1	RET	SPTA1	VHL
AR	CALR	CUL3	ERG	FUBP1	IDH2	MAML1	NFKBIA	PIK3R2	REV3L	SRC	VTCN1
ARAF	CARD11	CUL4A	ERRFI1	FZD1	IGF1	MAP2K1	NKX2-1	PIK3R3	RFC1	SRCAP	WAS
ARID1A	CASP8	CXCR2	ESR1	FZD10	IGF1R	MAP2K2	NKX3-1	PIM1	RHEB	SRSF2	WEE1
ARID1B	CBFB	CXCR4	ETV1	FZD2	IGF2	MAP2K4	NOTCH1	PLCG2	RHOA	STAG2	WRN
ARID2	CBL	CYLD	ETV4	FZD3	IGF2R	MAP3K1	NOTCH2	PMAIP1	RICTOR	STAT3	WT1
ARID5B	CCND1	CYP17A1	ETV5	FZD4	IKBKE	MAP3K13	NOTCH3	PMS1	RIF1	STK11	XIAP
ASXL1	CCND2	DAXX	ETV6	FZD5	IKZF1	MAPK1	NOTCH4	PMS2	RIT1	STN1	XPA
ASXL2	CCND3	DDIT3	EWSR1	FZD6	IL10	MAPK3	NPM1	POLD1	RNF43	SUFU	XPC
ATM	CCNE1	DDR1	EXO1	FZD7	IL6ST	MAX	NRAS	POLE	ROS1	SUZ12	XPO1
ATR	CD22	DDR2	EZH2	FZD8	IL7R	MCL1	NSD1	POLG	RPA1	SYK	XRCC1
ATRX	CD274	DICER1	FANCA	FZD9	INHBA	MDC1	NSD2	POLQ	RPS6KA3	TAF1	XRCC2
AURKA	CD276	DIS3	FANCC	GABRA6	INPP4B	MDM2	NSD3	PPARG	RPS6KA4	TBX3	XRCC3
AURKB	CD70	DNMT1	FANCD2	GATA1	INSR	MDM4	NTRK1	PPM1D	RPS6KB2	TCF3	XRCC4
AXIN1	CD79A	DNMT3A	FANCE	GATA2	IRF2	MED12	NTRK2	PPP2R1A	RPTOR	TCF7L2	XRCC5
AXIN2	CD79B	DNMT3B	FANCF	GATA3	IRF4	MEF2B	NTRK3	PPP2R2A	RUNX1	TEK	XRCC6
AXL	CDC73	DOT1L	FANCG	GATA4	IRS1	MEN1	NUP93	PPP6C	RUNX1T1	TEN1	YAP1
B2M	CDH1	E2F3	FANCI	GATA6	IRS2	MERTK	NUTM1	PRDM1	SDHA	TENT5C	YES1
BAP1	CDK12	EED	FANCL	GLI1	JAK1	MET	PAK1	PREX2	SDHAF2	TERC	ZNF217
BARD1	CDK2	EEF1A1	FANCM	GNA11	JAK2	MITF	PAK5	PRKAR1A	SDHB	TERT	ZRSR2
BAX	CDK4	EGFR	FAS	GNA13	JAK3	MLC1	PALB2	PRKDC	SDHC	TET1	
BBC3	CDK6	EIF1AX	FAT1	GNAQ	JUN	MLH1	PARG	PRKN	SDHD	TET2	
BCL10	CDK8	EIF4E	FBXW7	GNAS	KAT6A	MLH3	PARP1	PTCH1	SETBP1	TGFBR1	
BCL2	CDKN1A	ELF3	FGF10	GPC3	KDM5A	MPL	PARP2	PTEN	SETD2	TGFBR2	
BCL2L1	CDKN1B	EML4	FGF12	GREM1	KDM5C	MRE11	PAX5	PTK2	SF3B1	TLR4	
BCL2L11	CDKN2A	EMSY	FGF14	GRIN2A	KDM6A	MSH2	PAX8	PTPN11	SGK1	TLR7	
BCL2L2	CDKN2B	EP300	FGF19	GSK3B	KDR	MSH3	PAXIP1	PTPRD	SH2D1A	TLR8	

12 genes for the detection of amplifications

CCND1	CD274	CDK4	EGFR	ERBB2	FGF19	FGF3	FGF4	FGFR1	MDM2	MET	MYC

12 genes for the detection of translocations

ALK	BRAF	ETV6	EWSR1	FGFR2	FGFR3	NTRK1	NTRK2	NTRK3	RET	ROS1	TMPRSS2