

ABOUT THE TEST FoundationOne®Liquid CDx is a next generation sequencing (NGS) assay that identifies clinically relevant genomic alterations in circulating cell-free DNA.

PATIENT	DISEASE Stomach adenocarcinoma (NOS)	PHYSICIAN	ORDERING PHYSICIAN Yeh, Yi-Chen	SPECIMEN	SPECIMEN ID MCL 11/26/1964
	NAME Lin, Ming-Chih		MEDICAL FACILITY Taipei Veterans General Hospital		SPECIMEN TYPE Blood
	DATE OF BIRTH 26 November 1964		ADDITIONAL RECIPIENT None		DATE OF COLLECTION 25 January 2022
	SEX Male		MEDICAL FACILITY ID 205872		SPECIMEN RECEIVED 29 January 2022
	MEDICAL RECORD # 48102847		PATHOLOGIST Not Provided		

Biomarker Findings

Blood Tumor Mutational Burden - 1 Muts/Mb
Microsatellite status - MSI-High Not Detected
Tumor Fraction - Elevated Tumor Fraction Not Detected

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

GNAS R201H
TP53 E358V

† See About the Test in appendix for details.

Report Highlights

- There are no highlights associated with this patient's genomic findings.

For more information on potential biological and clinical significance, see the Biomarker and Genomic Findings sections.

BIOMARKER FINDINGS

Blood Tumor Mutational Burden - 1 Muts/Mb

Microsatellite status - MSI-High Not Detected

Tumor Fraction - Elevated Tumor Fraction Not Detected

THERAPY AND CLINICAL TRIAL IMPLICATIONS

No therapies or clinical trials. See Biomarker Findings section

MSI-High not detected. No evidence of microsatellite instability in this sample (see Appendix section).

Tumor fraction is considered elevated when ctDNA levels are high enough that aneuploidy can be detected. The fact that elevated tumor fraction was not detected in this specimen indicates the possibility of lower levels of ctDNA but does not compromise confidence in any reported alterations. However, in the setting of a negative liquid biopsy result, orthogonal testing of a tissue specimen should be considered if clinically indicated (see Biomarker Findings section).

No therapies or clinical trials are associated with the Genomic Findings for this sample.

If you have questions or comments about this result, please contact your Foundation Medicine customer support representative.

Phone: 1-888-988-3639
Online: foundationmedicine.com
Email: client.services@foundationmedicine.com

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

GENOMIC FINDINGS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIAL OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Findings section.

GNAS - R201H **p. 5** **TP53 - E358V** **p. 6**

NOTE Genomic alterations detected may be associated with activity of certain approved therapies; however, the therapies listed in this report may have varied clinical evidence in the patient's tumor type. Therapies and the clinical trials listed in this report may not be complete and/or exhaustive. Neither the therapies nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type. This report should be regarded and used as a supplementary source of information and not as the single basis for the making of a therapy decision. All treatment decisions remain the full and final responsibility of the treating physician and physicians should refer to approved prescribing information for all therapies. Therapies contained in this report may have been approved by the US FDA or other national authorities; however, they might not have been approved in your respective country. In the appropriate clinical context, germline testing of APC, ATM, BAP1, BRCA1, BRCA2, BRIP1, CHEK2, FH, FLCN, MEN1, MLH1, MSH2, MSH6, MUTYH, NF1, NF2, PALB2, PMS2, POLE, PTEN, RAD51C, RAD51D, RB1, RET, SDHA, SDHB, SDHC, SDHD, SMAD4, STK11, TGFBR2, TP53, TSC1, TSC2, VHL, and WT1 is recommended.

Variant Allele Frequency is not applicable for copy number alterations.

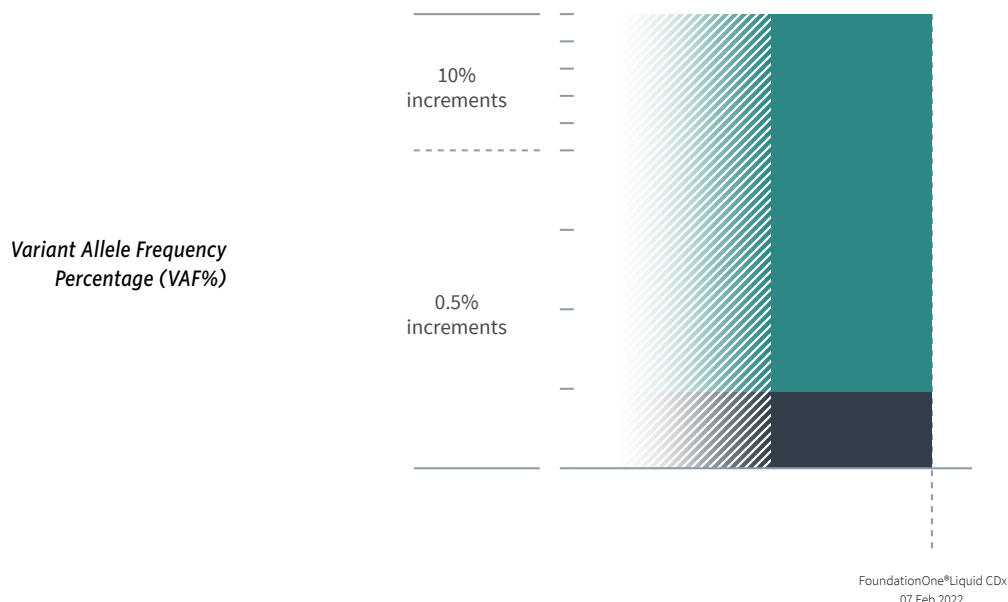
Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01



HISTORIC PATIENT FINDINGS		ORD-1289649-01 VAF%
Blood Tumor Mutational Burden		1 Muts/Mb
Microsatellite status		MSI-High Not Detected
Tumor Fraction		Elevated Tumor Fraction Not Detected
GNAS	● R201H	0.48%
TP53	● E358V	51.4%

NOTE This comparison table refers only to genes and biomarkers assayed by prior FoundationOne®Liquid CDx, FoundationOne®Liquid, FoundationOne®, or FoundationOne®CDx tests. Up to five previous tests may be shown.

For some genes in FoundationOne Liquid CDx, only select exons are assayed. Therefore, an alteration found by a previous test may not have been confirmed despite overlapping gene lists. Please refer to the Appendix for the complete list of genes and exons assayed. The gene and biomarker list will be updated periodically to reflect new knowledge about cancer biology.

As new scientific information becomes available, alterations that had previously been listed as Variants of Unknown Significance (VUS) may become reportable.

Tissue Tumor Mutational Burden (TMB) and blood TMB (bTMB) are estimated from the number of synonymous and non-synonymous single-nucleotide variants (SNVs) and insertions and deletions (indels) per area of coding genome sampled, after the removal of known and likely oncogenic driver events and germline SNPs. Tissue TMB is calculated based on variants with an allele frequency of $\geq 5\%$, and bTMB is calculated based on variants with an allele frequency of $\geq 0.5\%$.

Not Tested = not baited, not reported on test, or test preceded addition of biomarker or gene

Not Detected = baited but not detected on test

Detected = present (VAF% is not applicable)

VAF% = variant allele frequency percentage

Cannot Be Determined = Sample is not of sufficient data quality to confidently determine biomarker status

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

BIOMARKER FINDINGS
BIOMARKER

Blood Tumor Mutational Burden

RESULT
 1 Muts/Mb

POTENTIAL TREATMENT STRATEGIES
— Targeted Therapies —

On the basis of clinical evidence in NSCLC and HSNCC, increased bTMB may be associated with greater sensitivity to immunotherapeutic agents, including anti-PD-L1¹⁻² and anti-PD-1³ therapies. In NSCLC, multiple clinical trials have shown patients with higher bTMB derive clinical benefit from immune checkpoint inhibitors following single agent or combination treatments with either CTLA4 inhibitors or chemotherapy, with reported high bTMB cutpoints ranging from 6 to 16 Muts/Mb¹. In HNSCC, a Phase 3 trial showed

that bTMB ≥ 16 Muts/Mb (approximate equivalency ≥ 8 Muts/Mb as measured by this assay) was associated with improved survival from treatment with a PD-L1 inhibitor alone or in combination with a CTLA-4 inhibitor⁴.

FREQUENCY & PROGNOSIS

Average bTMB levels in solid tumors other than NSCLC have not been evaluated (cBioPortal, COSMIC, PubMed, Mar 2021)⁵⁻⁷. For patients with gastric cancer, increased TMB is reported to be associated with prolonged OS⁸⁻¹⁰. One study observed that the OS and disease-free survival (DFS) benefits of postoperative chemotherapy were more pronounced in patients with TMB-low gastric cancer (stage Ib/II) compared to those with TMB-high; however, patients with stage III gastric cancer benefitted regardless of TMB level¹¹. In esophageal cancer, patients with TMB-high who had not received radiotherapy had significantly reduced OS ($p=0.038$) compared to those with TMB-low¹².

FINDING SUMMARY

Blood tumor mutational burden (bTMB, also known as mutation load) is a measure of the number of somatic protein-coding base substitution and insertion/deletion mutations from circulating tumor DNA in blood. TMB is affected by a variety of causes, including exposure to mutagens such as ultraviolet light in melanoma¹³⁻¹⁴ and cigarette smoke in lung cancer¹⁵⁻¹⁶, treatment with temozolomide-based chemotherapy in glioma¹⁷⁻¹⁸, mutations in the proofreading domains of DNA polymerases encoded by the POLE and POLD1 genes¹⁹⁻²³, and microsatellite instability (MSI)^{19,22-23}. High bTMB levels were not detected in this sample. It is unclear whether the bTMB levels in this sample would be predicted to be associated with sensitivity to PD-1- or PD-L1-targeting immune checkpoint inhibitors, alone or in combination with other agents¹⁻³. Depending on the clinical context, TMB testing of an alternate sample or by another methodology could be considered.

BIOMARKER

Tumor Fraction

RESULT
 Elevated Tumor Fraction Not Detected

POTENTIAL TREATMENT STRATEGIES
— Targeted Therapies —

Specimens with elevated tumor fraction values have high circulating-tumor DNA (ctDNA) content, and thus high sensitivity for identifying genomic alterations. Such specimens are at low risk of false negative results. However, if elevated tumor fraction is not detected, it does not exclude the presence of disease burden or compromise the confidence of reported alterations. Tumor fraction levels currently have limited implications for diagnosis, surveillance, or therapy and should not

be overinterpreted or compared from one blood draw to another. There are currently no targeted approaches to address specific tumor fraction levels. In the research setting, changes in tumor fraction estimates have been associated with treatment duration and clinical response and may be a useful indicator for future cancer management²⁴⁻²⁹.

FREQUENCY & PROGNOSIS

Detectable ctDNA levels have been reported in a variety of tumor types, with higher tumor fraction levels reported for patients with metastatic (Stage 4) tumors compared with patients with localized disease (Stages 1 to 3)³⁰. Elevated tumor fraction levels have been reported to be associated with worse prognosis in a variety of cancer types, including pancreatic cancer³¹, Ewing sarcoma and osteosarcoma³², prostate cancer²⁷, breast cancer³³, leiomyosarcoma³⁴, esophageal cancer³⁵, colorectal

cancer³⁶, and gastrointestinal cancer³⁷.

FINDING SUMMARY

Tumor fraction provides an estimate of the percentage of ctDNA present in a cell-free DNA (cfDNA) sample. The tumor fraction estimate for this sample is based on the observed level of aneuploid instability. The tumor fraction algorithm utilized for FoundationOne Liquid CDx uses the allele frequencies of approximately 1,000 single-nucleotide polymorphism (SNP) sites across the genome. Unlike the maximum somatic allele frequency (MSAF) method of estimating ctDNA content³⁸, the tumor fraction metric does not take into account the allele frequency of individual variants but rather produces a more holistic estimate of ctDNA content using data from across the genome. The amount of ctDNA detected may correlate with disease burden and response to therapy³⁹⁻⁴⁰.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

GENOMIC FINDINGS

GENE

GNAS

ALTERATION

R201H

TRANSCRIPT ID

NM_000516

CODING SEQUENCE EFFECT

602G>A

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no therapies targeted to GNAS mutation in cancer. However, there is limited data indicating that a patient with appendiceal adenocarcinoma and a GNAS mutation (R201H) benefited from trametinib for 4 months⁴¹. Additionally, a patient with GNAS-mutated Erdheim-Chester disease exhibited a PR following treatment with single-agent trametinib⁴².

FREQUENCY & PROGNOSIS

The highest incidences of GNAS mutations have been reported in intraductal papillary mucinous neoplasms (40–66%)^{43–44} and appendiceal mucinous neoplasms (50–72%)^{45–46} as well as in tumors affecting the peritoneum (22%), pituitary gland (20%), bone (14%), pancreas (11%), and small intestine (11%)(COSMIC, 2022)⁷. Amplification of GNAS has been reported in ovarian epithelial carcinomas (12–30%)^{47–49}, colorectal adenocarcinoma (9%)²², stomach adenocarcinoma (7%)⁵⁰, lung adenocarcinoma (6.5%)⁵¹, breast invasive carcinoma (6.5%)⁵², pancreatic adenocarcinoma (6%)⁵³, and sarcomas (5.8%)⁵⁴. GNAS mutations are rare in hematological malignancies generally (COSMIC, 2022)^{7,55–56}. Activating GNAS mutations have been identified in gastrointestinal polyps in 75% (3/4) of patients with McCune-Albright syndrome⁵⁷. Amplification of GNAS has been associated with shorter progression-free survival in patients with ovarian cancer^{48–49}, while activating GNAS mutations have been correlated with tumor progression and poor

prognosis in patients with gastric cancer⁵⁸.

FINDING SUMMARY

GNAS encodes the alpha subunit of the stimulatory G protein (Gs-alpha)⁵⁹. Gs-alpha is a guanine-nucleotide binding protein (G protein) that is involved in hormonal regulation of adenylate cyclase⁵⁹. GNAS has been reported to be amplified in cancer⁶ and may be biologically relevant in this context^{60–61}. GNAS alterations that have been shown to result in constitutive activation of adenylyl cyclase and an increase in cellular cAMP concentration^{62–67} are predicted to be activating. Mutations at R201 specifically are commonly associated with McCune-Albright syndrome, a disease that can co-occur with various cancers in patients with GNAS activating mutations^{68–70}.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. • 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

GENOMIC FINDINGS

GENE

TP53

ALTERATION
E358V

TRANSCRIPT ID
NM_000546

CODING SEQUENCE EFFECT
1073A>T

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no approved therapies to address TP53 mutation or loss. However, tumors with TP53 loss of function alterations may be sensitive to the WEE1 inhibitor adavosertib⁷¹⁻⁷⁴, or p53 gene therapy and immunotherapeutics such as SGT-53⁷⁵⁻⁷⁹ and ALT-801⁸⁰. In a Phase 1 study, adavosertib in combination with gemcitabine, cisplatin, or carboplatin elicited PRs in 9.7% and SDs in 53% of patients with solid tumors; the response rate was 21% (4/19) for patients with TP53 mutations versus 12% (4/33) for patients who were TP53 wildtype⁸¹. A Phase 2 trial of adavosertib in combination with chemotherapy (gemcitabine, carboplatin, paclitaxel, or doxorubicin) reported a 32% (30/94, 3 CR) ORR and a 73% (69/94) DCR for patients with platinum-refractory TP53-mutated ovarian, Fallopian tube, or peritoneal cancer⁸². A smaller Phase 2 trial of adavosertib in combination with carboplatin achieved a 43% (9/21, 1 CR) ORR and a 76% (16/21) DCR for patients with platinum-refractory TP53-mutated ovarian cancer⁸³. The combination of adavosertib with paclitaxel and carboplatin for patients with TP53-mutated ovarian cancer also significantly increased PFS compared with paclitaxel and carboplatin alone⁸⁴. In the Phase 2 VIKTORY trial, patients with TP53-mutated metastatic and/or recurrent gastric cancer experienced a 24% (6/25) ORR with adavosertib combined with paclitaxel⁸⁵. A Phase 1 trial of neoadjuvant adavosertib in combination with cisplatin and docetaxel for head and neck squamous cell carcinoma (HNSCC) elicited a 71% (5/7) response rate for patients with TP53

alterations⁸⁶. The Phase 2 FOCUS4-C trial for patients with TP53- and RAS-mutated colorectal cancer reported improvement in PFS (3.61 vs. 1.87 months, HR=0.35, p=0.0022), but not OS (14.0 vs 12.8 months, p=0.93), following adavosertib treatment compared with active monitoring⁸⁷. In a Phase 1b clinical trial of SGT-53 in combination with docetaxel for patients with solid tumors, 75% (9/12) of evaluable patients experienced clinical benefit, including 2 confirmed and 1 unconfirmed PRs and 2 instances of SD with significant tumor shrinkage⁷⁹. Missense mutations leading to TP53 inactivation may also be sensitive to therapies that reactivate mutated p53 such as APR-246⁸⁸⁻⁹⁰. In a Phase 1b trial for patients with p53-positive high-grade serous ovarian cancer, APR-246 combined with carboplatin and pegylated liposomal doxorubicin achieved a 52% (11/21) response rate and 100% DCR⁹¹. ATR inhibitor treatment of chronic lymphocytic leukemia (CLL) cells with biallelic inactivation of TP53 suppressed cell viability, promoted DNA damage, and attenuated xenograft growth in preclinical studies⁹²⁻⁹³; however, ATR inhibitors as monotherapy had little effect on these parameters in solid tumor models in other preclinical studies⁹⁴⁻⁹⁵. Therefore, it is unclear whether TP53 inactivation predicts sensitivity to ATR inhibition. It is not known whether these therapeutic approaches would be relevant in the context of alterations that have not been fully characterized, as seen here.

FREQUENCY & PROGNOSIS

TP53 is frequently mutated in cancers of the gastrointestinal tract, with alterations reported in 34–72% of esophageal, gastroesophageal junction, and gastric adenocarcinomas^{50,96-98}. Overexpression of p53 protein, which may occur as a result of mutation, has been reported in approximately 36% of gastric cancers, with p53 expression reported to be more frequent in intestinal-type compared with diffuse-type gastric cancer⁹⁹⁻¹⁰². While some studies have reported no association between TP53 mutation status and prognosis in patients with esophageal carcinoma or gastroesophageal junction adenocarcinoma⁹⁷⁻⁹⁸ others have associated TP53 mutation and elevated p53 expression with poor prognosis for patients

with esophageal squamous cell carcinoma¹⁰³⁻¹⁰⁴ or stomach cancer¹⁰⁵⁻¹⁰⁷.

FINDING SUMMARY

Functional loss of the tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers¹⁰⁸. Although alterations such as seen here have not been fully characterized and are of unknown functional significance, similar alterations have been previously reported in the context of cancer, which may indicate biological relevance.

POTENTIAL GERMLINE IMPLICATIONS

Germline mutations in TP53 are associated with the very rare autosomal dominant disorder Li-Fraumeni syndrome and the early onset of many cancers¹⁰⁹⁻¹¹¹, including sarcomas¹¹²⁻¹¹³. Estimates for the prevalence of germline TP53 mutations in the general population range from 1:5,000¹¹⁴ to 1:20,000¹¹³. For pathogenic TP53 mutations identified during tumor sequencing, the rate of germline mutations was 1% in the overall population and 6% in tumors arising before age 30¹¹⁵. In the appropriate clinical context, germline testing of TP53 is recommended.

POTENTIAL CLONAL HEMATOPOIESIS IMPLICATIONS

Variants seen in this gene have been reported to occur in clonal hematopoiesis (CH), an age-related process in which hematopoietic stem cells acquire somatic mutations that allow for clonal expansion¹¹⁶⁻¹²¹. CH in this gene has been associated with increased mortality, risk of coronary heart disease, risk of ischemic stroke, and risk of secondary hematologic malignancy¹¹⁶⁻¹¹⁷. Clinical management of patients with CH in this gene may include monitoring for hematologic changes and reduction of controllable risk factors for cardiovascular disease¹²². Comprehensive genomic profiling of solid tumors detects nontumor alterations that are due to CH^{120,123-124}. Patient-matched peripheral blood mononuclear cell sequencing is required to conclusively determine if this alteration is present in tumor or is secondary to CH.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. • 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX
Variants of Unknown Significance

NOTE One or more variants of unknown significance (VUS) were detected in this patient's tumor. These variants may not have been adequately characterized in the scientific literature at the time this report was issued, and/or the genomic context of these alterations makes their significance unclear. We choose to include them here in the event that they become clinically meaningful in the future.

CALR
P243L

CD22
V267I

FGFR1
R80C

KMT2A (MLL)
A53V

LTK
splice site 997+1G>A

MLL2
P2349L

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX
Genes assayed in FoundationOne®Liquid CDx

FoundationOne Liquid CDx interrogates 324 genes, including 309 genes with complete exonic (coding) coverage and 15 genes with only select non-coding coverage (indicated with an *); 75 genes (indicated in bold) are captured with increased sensitivity and have complete exonic (coding) coverage unless otherwise noted.

ABL1 Exons 4-9	ACVR1B	AKT1 Exon 3	AKT2	AKT3	ALK Exons 20-29, Introns 18, 19	ALOX12B	AMER1 (FAM123B)	APC
AR	ARAF Exons 4, 5, 7, 11, 13, 15, 16	ARFRP1	ARID1A	ASXL1	ATM	ATR	ATRX	AURKA
AURKB	AXIN1	AXL	BAP1	BARD1	BCL2	BCL2L1	BCL2L2	BCL6
BCOR	BCORL1	BCR* Introns 8, 13, 14	BRAF Exons 11-18, Introns 7-10	BRCA1 Introns 2, 7, 8, 12, 16, 19, 20	BRCA2 Intron 2	BRD4	BRIP1	BTG1
BTG2	BTK Exons 2, 15	C11orf30 (EMSY)	C17orf39 (GID4)	CALR	CARD11	CASP8	CBFB	CBL
CCND1	CCND2	CCND3	CCNE1	CD22	CD70	CD74* Introns 6-8	CD79A	CD79B
CD274 (PD-L1)	CDC73	CDH1	CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B
CDKN2A	CDKN2B	CDKN2C	CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL
CSF1R	CSF3R	CTCF	CTNNA1	CTNNB1 Exon 3	CUL3	CUL4A	CXCR4	CYP17A1
DAXX	DDR1	DDR2 Exons 5, 17, 18	DIS3	DNMT3A	DOT1L	EED	EGFR Introns 7, 15, 24-27	EP300
EPHA3	EPHB1	EPHB4	ERBB2	ERBB3 Exons 3, 6, 7, 8, 10, 12, 20, 21, 23, 24, 25	ERBB4	ERCC4	ERG	ERRFI1
ESR1 Exons 4-8	ETV4* Intron 8	ETV5* Introns 6, 7	ETV6* Introns 5, 6	EWSR1* Introns 7-13	EZH2 Exons 4, 16, 17, 18	EZR* Introns 9-11	FAM46C	FANCA
FANCC	FANCG	FANCL	FAS	FBXW7	FGF10	FGF12	FGF14	FGF19
FGF23	FGF3	FGF4	FGF6	FGFR1 Introns 1, 5, Intron 17	FGFR2 Intron 1, Intron 17	FGFR3 Exons 7, 9 (alternative designation exon 10), 14, 18, Intron 17	FGFR4	FH
FLCN	FLT1	FLT3 Exons 14, 15, 20	FOXL2	FUBP1	GABRA6	GATA3	GATA4	GATA6
GNA11 Exons 4, 5	GNA13	GNAQ Exons 4, 5	GNAS Exons 1, 8	GRM3	GSK3B	H3F3A	HDAC1	HGF
HNFI1A	HRAS Exons 2, 3	HSD3B1	ID3	IDH1 Exon 4	IDH2 Exon 4	IGF1R	IKBKE	IKZF1
INPP4B	IRF2	IRF4	IRS2	JAK1	JAK2 Exon 14	JAK3 Exons 5, 11, 12, 13, 15, 16	JUN	KDM5A
KDM5C	KDM6A	KDR	KEAP1	KEL	KIT Exons 8, 9, 11, 12, 13, 17, Intron 16	KLHL6	KMT2A (MLL) Introns 6, 8-11, Intron 7	KMT2D (MLL2)

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX

Genes assayed in FoundationOne®Liquid CDx

FoundationOne Liquid CDx interrogates 324 genes, including 309 genes with complete exonic (coding) coverage and 15 genes with only select non-coding coverage (indicated with an *); 75 genes (indicated in bold) are captured with increased sensitivity and have complete exonic (coding) coverage unless otherwise noted.

KRAS	LTK	LYN	MAF	MAP2K1 (MEK1) Exons 2, 3	MAP2K2 (MEK2) Exons 2-4, 6, 7	MAP2K4	MAP3K1	MAP3K13
MAPK1	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1	MERTK	MET
MITF	MKNK1	MLH1	MPL Exon 10	MRE11A	MSH2 Intron 5	MSH3	MSH6	MST1R
MTAP	MTOR Exons 19, 30, 39, 40, 43-45, 47, 48, 53, 56	MUTYH	MYB* Intron 14	MYC Intron 1	MYCL (MYCL1)	MYCN	MYD88 Exon 4	NBN
NF1	NF2	NFE2L2	NFKBIA	NKX2-1	NOTCH1	NOTCH2 Intron 26	NOTCH3	NPM1 Exons 4-6, 8, 10
NRAS Exons 2, 3	NSD3 (WHSC1L1)	NTSC2	NTRK1 Exons 14, 15, Introns 8-11	NTRK2 Intron 12	NTRK3 Exons 16, 17	NUTM1* Intron 1	P2RY8	PALB2
PARK2	PARP1	PARP2	PARP3	PAX5	PBRM1	PDCD1 (PD-1)	PDCD1LG2 (PD-L2)	PDGFRA Exons 12, 18, Introns 7, 9, 11
PDGFRB Exons 12-21, 23	PDK1	PIK3C2B	PIK3C2G	PIK3CA Exons 2, 3, 5-8, 10, 14, 19, 21 (Coding Exons 1, 2, 4-7, 9, 13, 18, 20) PPP2R2A	PIK3CB	PIK3R1	PIM1	PMS2
POLD1	POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI	PTCH1
PTEN	PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RAF1 Exons 3, 4, 6, 7, 10, 14, 15, 17, Introns 4-8	RARA Intron 2	RB1	RBM10	REL	RET Introns 7, 8, Exons 11, 13-16, Introns 9-11
RICTOR	RNF43	ROS1 Exons 31, 36-38, 40, Introns 31-35	RPTOR	RSP02* Intron 1	SDC4* Intron 2	SDHA	SDHB	SDHC
SDHD	SETD2	SF3B1	SGK1	SLC34A2* Intron 4	SMAD2	SMAD4	SMARCA4	SMARCB1
SMO	SNCAIP	SOC1	SOX2	SOX9	SPEN	SPOP	SRC	STAG2
STAT3	STK11	SUFU	SYK	TBX3	TEK	TERC* ncRNA	TERT* Promoter	TET2
TGFBR2	TIPARP	TMPRSS2* Introns 1-3	TNFAIP3	TNFRSF14	TP53	TSC1	TSC2	TYRO3
U2AF1	VEGFA	VHL	WHSC1	WT1	XPO1	XRCC2	ZNF217	ZNF703

ADDITIONAL ASSAYS: FOR THE DETECTION OF SELECT CANCER BIOMARKERS

Microsatellite (MS) status

Blood Tumor Mutational Burden (bTMB)

Tumor Fraction

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX

About FoundationOne®Liquid CDx

FoundationOne Liquid CDx fulfills the requirements of the European Directive 98/79 EC for in vitro diagnostic medical devices and is registered as a CE-IVD product by Foundation Medicine's EU Authorized Representative, Qarad b.v.b.a, Cipalstraat 3, 2440 Geel, Belgium. The CE-IVD regulatory status of FoundationOne Liquid CDx is applicable in countries that accept and/or recognize the CE mark.



ABOUT FOUNDATIONONE LIQUID CDx

FoundationOne Liquid CDx was developed and its performance characteristics determined by Foundation Medicine, Inc. (Foundation Medicine). FoundationOne Liquid CDx may be used for clinical purposes and should not be regarded as purely investigational or for research only. Foundation Medicine's clinical reference laboratories are qualified to perform high-complexity clinical testing.

Please refer to technical information for performance specification details.

INTENDED USE

FoundationOne Liquid CDx is a next generation sequencing based *in vitro* diagnostic device that analyzes 324 genes. Substitutions and insertion and deletion alterations (indels) are reported in 311 genes, copy number alterations (CNAs) are reported in 310 genes, and gene rearrangements are reported in 324 genes. The test also detects the genomic signatures blood tumor mutational burden (bTMB), microsatellite instability (MSI), and tumor fraction. FoundationOne Liquid CDx utilizes circulating cell-free DNA (cfDNA) isolated from plasma derived from the anti-coagulated peripheral whole blood of cancer patients. The test is intended to be used as a companion diagnostic to identify patients who may benefit from treatment with targeted therapies in accordance with the approved therapeutic product labeling. Additionally, FoundationOne Liquid CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with malignant neoplasms.

TEST PRINCIPLES

The FoundationOne Liquid CDx assay is performed exclusively as a laboratory service using circulating cell-free DNA (cfDNA) isolated from plasma derived from anti-coagulated peripheral whole blood from patients with solid malignant neoplasms. The assay employs a single DNA extraction method to obtain cfDNA from plasma from whole blood. Extracted

cfDNA undergoes whole-genome shotgun library construction and hybridization-based capture of 324 cancer-related genes including coding exons and select introns of 309 genes, as well as only select intronic regions or non-coding regions of 15 genes. Hybrid-capture selected libraries are sequenced with deep coverage using the NovaSeq® 6000 platform. Sequence data are processed using a customized analysis pipeline designed to accurately detect genomic alterations, including base substitutions, indels, select copy number variants, and select genomic rearrangements. Substitutions and insertion and deletion alterations (indels) are reported in 311 genes, copy number alterations (CNAs) are reported in 310 genes, and gene rearrangements are reported in 324 genes. The assay also reports tumor fraction, and genomic signatures including MSI and bTMB. A subset of targeted regions in 75 genes is baited for increased sensitivity.

THE REPORT

Incorporates analyses of peer-reviewed studies and other publicly available information identified by Foundation Medicine; these analyses and information may include associations between a molecular alteration (or lack of alteration) and one or more drugs with potential clinical benefit (or potential lack of clinical benefit), including drug candidates that are being studied in clinical research. *Note:* A finding of biomarker alteration does not necessarily indicate pharmacologic effectiveness (or lack thereof) of any drug or treatment regimen; a finding of no biomarker alteration does not necessarily indicate lack of pharmacologic effectiveness (or effectiveness) of any drug or treatment regimen.

QUALIFIED ALTERATION CALLS (EQUIVOCAL)

All equivocal calls, regardless of alteration type, imply that there is adequate evidence to call the alteration with confidence. However, the repeatability of equivocal calls may be lower than non-equivocal calls.

RANKING OF THERAPIES AND CLINICAL TRIALS

Ranking of Therapies in Summary Table

Therapies are ranked based on the following criteria: Therapies with clinical benefit (ranked alphabetically within each evidence category), followed by therapies associated with resistance (when applicable).

Ranking of Clinical Trials

Pediatric trial qualification → Geographical proximity → Later trial phase.

LIMITATIONS

1. For *in vitro* diagnostic use.
2. For prescription use only. This test must be ordered by a qualified medical professional in accordance with clinical laboratory regulations.
3. A negative result does not rule out the presence of a mutation below the limits of detection of the assay. Patients for whom no companion diagnostic alterations are detected should be considered for confirmation with an appropriately validated tumor tissue test, if available.
4. The FoundationOne Liquid CDx assay does not detect heterozygous deletions.
5. The test is not intended to provide information on cancer predisposition.
6. Performance has not been validated for cfDNA input below the specified minimum input.
7. Tissue TMB and blood TMB (bTMB) are estimated from the number of synonymous and nonsynonymous single-nucleotide variants (SNVs) and insertions and deletions (indels) per area of coding genome sampled, after the removal of known and likely oncogenic driver events and germline SNPs. Tissue TMB is calculated based on variants with an allele frequency of $\geq 5\%$, and bTMB is calculated based on variants with an allele frequency of $\geq 0.5\%$.
8. Tumor fraction is the percentage of circulating tumor DNA (ctDNA) present in a cell-free DNA (cfDNA) sample. The tumor fraction estimate is computationally derived from the observed level of aneuploidy in the sample. Tumor fraction is considered elevated when ctDNA levels are high enough that aneuploidy can be detected and is significantly distinct from that typically found in non-tumor samples.
9. Microsatellite instability (MSI) is a condition of genetic hypermutability that generates excessive amounts of short insertion/deletion mutations in the tumor genome; it generally occurs at microsatellite DNA sequences and is caused by a deficiency in DNA mismatch repair (MMR) in the tumor. The MSI algorithm is based on genome wide analysis of 1765 microsatellite loci and not based on the 5 or 7 MSI loci described in current clinical practice guidelines for solid tissue testing.
10. Genomic findings from circulating cell-free DNA (cfDNA) may originate from circulating tumor DNA fragments, germline alterations, or non-tumor somatic alterations, such as clonal hematopoiesis of indeterminate potential (CHIP). Genes with alterations that may be derived from CHIP include, but are not limited

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX

About FoundationOne®Liquid CDx

to: *ASXL1*, *ATM*, *CBL*, *CHEK2*, *DNMT3A*, *JAK2*, *KMT2D* (*MLL2*), *MPL*, *MYD88*, *SF3B1*, *TET2*, *TP53*, and *U2AF1*.

11. Alterations reported may include somatic (not inherited) or germline (inherited) alterations; however, the test does not distinguish between germline and somatic alterations. If a reported alteration is suspected to be germline, confirmatory testing should be considered in the appropriate clinical context.
12. The test is not intended to replace germline testing or to provide information about cancer predisposition.

REPORT HIGHLIGHTS

The Report Highlights includes select genomic and therapeutic information with potential impact on patient care and treatment that is specific to the genomics and tumor type of the sample analyzed. This section may highlight information including targeted therapies with potential sensitivity or resistance; evidence-matched clinical trials; and variants with potential diagnostic, prognostic, nontargeted treatment, germline, or clonal hematopoiesis implications. Information included in the Report Highlights is expected to evolve with advances in scientific and clinical research. Findings included in the Report Highlights should be considered in the context of all other information in this report and other relevant patient information. Decisions on patient care and treatment are the responsibility of the treating physician.

VARIANTS TO CONSIDER FOR FOLLOW-UP GERMLINE TESTING

The variants indicated for consideration of follow-up germline testing are 1) limited to reportable short variants with a protein effect listed in the ClinVar genomic database (Landrum et al., 2018; 29165669) as Pathogenic, Pathogenic/Likely Pathogenic, or Likely Pathogenic (by an expert panel or multiple submitters), 2) associated with hereditary cancer-predisposing disorder(s), 3) detected at an allele frequency of >30%, and 4) in select genes reported by the ESMO Precision Medicine Working Group (Mandelker et al., 2019; 31050713) to have a greater than 10% probability of germline origin if identified during tumor sequencing. The selected genes are *ATM*, *BAP1*, *BRCA1*, *BRCA2*, *BRIP1*, *CHEK2*, *FH*, *FLCN*, *MLH1*, *MSH2*, *MSH6*, *MUTYH*, *PALB2*, *PMS2*, *POLE*, *RAD51C*, *RAD51D*, *RET*, *SDHA*, *SDHB*, *SDHC*, *SDHD*, *TSC2*, and *VHL*, and are not inclusive of all cancer susceptibility genes. The content in this report should not substitute for genetic counseling or follow-up germline testing, which is needed to

distinguish whether a finding in this patient's tumor sequencing is germline or somatic. Interpretation should be based on clinical context.

VARIANTS THAT MAY REPRESENT CLONAL HEMATOPOIESIS

Variants that may represent clonal hematopoiesis (CH) are limited to select reportable short variants in defined genes identified in solid tumors only. Variant selection was determined based on gene tumor-suppressor or oncogene status, known role in solid tumors versus hematological malignancies, and literature prevalence. The defined genes are *ASXL1*, *ATM*, *CBL*, *CHEK2*, *DNMT3A*, *IDH2*, *JAK2*, *KMT2D* (*MLL2*), *MPL*, *MYD88*, *SF3B1*, *TET2*, and *U2AF1* and are not inclusive of all CH genes. The content in this report should not substitute for dedicated hematological workup. Comprehensive genomic profiling of solid tumors detects nontumor alterations that are due to CH. Patient-matched peripheral blood mononuclear cell sequencing is required to conclusively determine if this alteration is present in tumor or is secondary to CH. Interpretation should be based on clinical context.

NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®) CATEGORIZATION

Biomarker and genomic findings detected may be associated with certain entries within the NCCN Drugs & Biologics Compendium® (NCCN Compendium®) (www.nccn.org). The NCCN Categories of Evidence and Consensus indicated reflect the highest possible category for a given therapy in association with each biomarker or genomic finding. Please note, however, that the accuracy and applicability of these NCCN categories within a report may be impacted by the patient's clinical history, additional biomarker information, age, and/or co-occurring alterations. For additional information on the NCCN categories, please refer to the NCCN Compendium®. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

LEVEL OF EVIDENCE NOT PROVIDED

Drugs with potential clinical benefit (or potential lack of clinical benefit) are not evaluated for source or level of published evidence.

NO GUARANTEE OF CLINICAL BENEFIT

This report makes no promises or guarantees that a particular drug will be effective in the treatment of disease in any patient. This report also makes no promises or guarantees that a drug with potential lack of clinical benefit will in fact provide no clinical benefit.

NO GUARANTEE OF REIMBURSEMENT

Foundation Medicine makes no promises or guarantees that a healthcare provider, insurer or other third party payor, whether private or governmental, will reimburse a patient for the cost of FoundationOne Liquid CDx.

TREATMENT DECISIONS ARE THE RESPONSIBILITY OF PHYSICIAN

Drugs referenced in this Report may not be suitable for a particular patient. The selection of any, all or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) resides entirely within the discretion of the treating physician. Indeed, the information in this Report must be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating physician recommends a course of treatment. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable 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 standard of care in a given community. A treating physician's decisions should not be based on a single test, such as this test or the information contained in this report.

Certain sample of variant characteristics may result in reduced sensitivity. These include: low sample quality, deletions and insertions >40bp, or repetitive/high homology sequences. FoundationOne Liquid CDx is performed using cell-free DNA, and as such germline events may not be reported.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. • 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX

About FoundationOne®Liquid CDx

SELECT ABBREVIATIONS

ABBREVIATION	DEFINITION
CR	Complete response
DCR	Disease control rate
DNMT	DNA methyltransferase
HR	Hazard ratio
ITD	Internal tandem duplication
MMR	Mismatch repair
Muts/Mb	Mutations per megabase
NOS	Not otherwise specified
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PFS	Progression-free survival
PR	Partial response
SD	Stable disease
TKI	Tyrosine kinase inhibitor

MR Suite Version 5.2.0

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1289649-01

APPENDIX
References

1. Gandara DR, et al. Nat. Med. (2018) PMID: 30082870
2. Wang Z, et al. JAMA Oncol (2019) PMID: 30816954
3. Aggarwal C, et al. Clin. Cancer Res. (2020) PMID: 32102950
4. Li et al., 2020; ASCO Abstract 6511
5. Cerami E, et al. Cancer Discov (2012) PMID: 22588877
6. Gao J, et al. Sci Signal (2013) PMID: 23550210
7. Tate JG, et al. Nucleic Acids Res. (2019) PMID: 30371878
8. Cai L, et al. Cancer Commun (Lond) (2020) PMID: 32141230
9. Zhao DY, et al. World J Gastrointest Oncol (2021) PMID: 33510848
10. Wei XL, et al. Ther Adv Med Oncol (2021) PMID: 33613701
11. Wang D, et al. Gastric Cancer (2021) PMID: 33687617
12. Yuan C, et al. Aging (Albany NY) (2020) PMID: 32165590
13. Pfeifer GP, et al. Mutat. Res. (2005) PMID: 15748635
14. Hill VK, et al. Annu Rev Genomics Hum Genet (2013) PMID: 23875803
15. Pfeifer GP, et al. Oncogene (2002) PMID: 12379884
16. Rizvi NA, et al. Science (2015) PMID: 25765070
17. Johnson BE, et al. Science (2014) PMID: 24336570
18. Choi S, et al. Neuro-oncology (2018) PMID: 29452419
19. Cancer Genome Atlas Research Network, et al. Nature (2013) PMID: 23636398
20. Briggs S, et al. J. Pathol. (2013) PMID: 23447401
21. Heitzer E, et al. Curr. Opin. Genet. Dev. (2014) PMID: 24583393
22. Nature (2012) PMID: 22810696
23. Roberts SA, et al. Nat. Rev. Cancer (2014) PMID: 25568919
24. Bronkhorst AJ, et al. Biomol Detect Quantif (2019) PMID: 30923679
25. Raja R, et al. Clin. Cancer Res. (2018) PMID: 30093454
26. Hrebien S, et al. Ann. Oncol. (2019) PMID: 30860573
27. Choudhury AD, et al. JCI Insight (2018) PMID: 30385733
28. Goodall J, et al. Cancer Discov (2017) PMID: 28450425
29. Goldberg SB, et al. Clin. Cancer Res. (2018) PMID: 29330207
30. Bettgeowda C, et al. Sci Transl Med (2014) PMID: 24553385
31. Lapin M, et al. J Transl Med (2018) PMID: 30400802
32. Shulman DS, et al. Br. J. Cancer (2018) PMID: 30131550
33. Stover DG, et al. J. Clin. Oncol. (2018) PMID: 29298117
34. Hemming ML, et al. JCO Precis Oncol (2019) PMID: 30793095
35. Egvud M, et al. Ann. Thorac. Surg. (2019) PMID: 31059681
36. Fan G, et al. PLoS ONE (2017) PMID: 28187169
37. Vu et al., 2020; DOI: 10.1200/PO.19.00204
38. Li G, et al. J Gastrointest Oncol (2019) PMID: 31602320
39. Zhang EW, et al. Cancer (2020) PMID: 32757294
40. Butler TM, et al. Cold Spring Harb Mol Case Stud (2019) PMID: 30833418
41. Ang C, et al. Case Rep Oncol () PMID: 28868010
42. Saunders IM, et al. Oncologist (2019) PMID: 31740567
43. Furukawa T, et al. Sci Rep (2011) PMID: 22355676
44. Wu J, et al. Sci Transl Med (2011) PMID: 21775669
45. Nishikawa G, et al. Br. J. Cancer (2013) PMID: 23403822
46. Singhi AD, et al. Hum. Pathol. (2014) PMID: 24925222
47. Nature (2011) PMID: 21720365
48. Kan Z, et al. Nature (2010) PMID: 20668451
49. Tominaga E, et al. Gynecol. Oncol. (2010) PMID: 20537689
50. Nature (2014) PMID: 25079317
51. Nature (2014) PMID: 25079552
52. Nature (2012) PMID: 23000897
53. Witkiewicz AK, et al. Nat Commun (2015) PMID: 25855536
54. Barretina J, et al. Nat. Genet. (2010) PMID: 20601955
55. Lohr JG, et al. Cancer Cell (2014) PMID: 24434212
56. Chapman MA, et al. Nature (2011) PMID: 21430775
57. Zacharin M, et al. J. Med. Genet. (2011) PMID: 21357941
58. Alakus H, et al. World J Gastroenterol. (2009) PMID: 20027678
59. Hayward BE, et al. Proc. Natl. Acad. Sci. U.S.A. (1998) PMID: 9860993
60. Zack TI, et al. Nat. Genet. (2013) PMID: 24071852
61. Beroukheim R, et al. Nature (2010) PMID: 20164920
62. Masters SB, et al. J. Biol. Chem. (1989) PMID: 2549064
63. Graziano MP, et al. J. Biol. Chem. (1989) PMID: 2549065
64. Jang IS, et al. Exp. Mol. Med. (2001) PMID: 11322485
65. Landis CA, et al. Nature (1989) PMID: 2549426
66. Tobar-Rubin R, et al. J. Mol. Endocrinol. (2013) PMID: 23288949
67. Mariot V, et al. Bone (2011) PMID: 20887824
68. Weinstein LS, et al. N. Engl. J. Med. (1991) PMID: 1944469
69. Collins MT, et al. J. Clin. Endocrinol. Metab. (2003) PMID: 12970318
70. Nault JC, et al. J. Hepatol. (2012) PMID: 21835143
71. Hirai H, et al. Cancer Biol. Ther. (2010) PMID: 20107315
72. Bridges KA, et al. Clin. Cancer Res. (2011) PMID: 21799033
73. Rajeshkumar NV, et al. Clin. Cancer Res. (2011) PMID: 21389100
74. Osman AA, et al. Mol. Cancer Ther. (2015) PMID: 25504633
75. Xu L, et al. Mol. Cancer Ther. (2002) PMID: 12489850
76. Xu L, et al. Mol. Med. (2001) PMID: 11713371
77. Camp ER, et al. Cancer Gene Ther. (2013) PMID: 23470564
78. Kim SS, et al. Nanomedicine (2015) PMID: 25240597
79. Pirolo KF, et al. Mol. Ther. (2016) PMID: 27357628
80. Hajdenberg et al., 2012; ASCO Abstract e15010
81. Leijen S, et al. J. Clin. Oncol. (2016) PMID: 27601554
82. Moore et al., 2019; ASCO Abstract 5513
83. Leijen S, et al. J. Clin. Oncol. (2016) PMID: 27998224
84. Oza et al., 2015; ASCO Abstract 5506
85. Lee J, et al. Cancer Discov (2019) PMID: 31315834
86. Méndez E, et al. Clin. Cancer Res. (2018) PMID: 29535125
87. Seligmann JF, et al. J Clin Oncol (2021) PMID: 34538072
88. Lehmann S, et al. J. Clin. Oncol. (2012) PMID: 22965953
89. Mohell N, et al. Cell Death Dis (2015) PMID: 26086967
90. Fransson Å, et al. J Ovarian Res (2016) PMID: 27179933
91. Gourley et al., 2016; ASCO Abstract 5571
92. Kwok M, et al. Blood (2016) PMID: 26563132
93. Boudny M, et al. Haematologica (2019) PMID: 30975914
94. Dillon MT, et al. Mol. Cancer Ther. (2017) PMID: 28062704
95. Middleton FK, et al. Cancers (Basel) (2018) PMID: 30127241
96. Dulak AM, et al. Nat. Genet. (2013) PMID: 23525077
97. Sengpiel C, et al. Cancer Invest. (2009) PMID: 19160092
98. Pühringer-Oppermann F, et al. J. Cancer Res. Clin. Oncol. (2006) PMID: 16538517
99. Lee HE, et al. Pathobiology (2014) PMID: 23969480
100. Sezer C, et al. J BUON () PMID: 23613399
101. Victorzon M, et al. Eur. J. Cancer (1996) PMID: 8664030
102. Gonçalves AR, et al. Pathol. Oncol. Res. (2011) PMID: 21116760
103. Han U, et al. Dis. Esophagus (2007) PMID: 17760650
104. Yamasaki M, et al. Ann. Surg. Oncol. (2010) PMID: 19941080
105. Liu X, et al. PLoS ONE (2012) PMID: 23285001
106. Wiksten JP, et al. Anticancer Res. () PMID: 18751407
107. Miglaviacca M, et al. J. Cell. Physiol. (2004) PMID: 15254976
108. Brown CJ, et al. Nat. Rev. Cancer (2009) PMID: 19935675
109. Bougeard G, et al. J. Clin. Oncol. (2015) PMID: 26014290
110. Sorrell AD, et al. Mol Diagn Ther (2013) PMID: 23355100
111. Nichols KE, et al. Cancer Epidemiol. Biomarkers Prev. (2001) PMID: 11219776
112. Kleihues P, et al. Am. J. Pathol. (1997) PMID: 9006316
113. Gonzalez KD, et al. J. Clin. Oncol. (2009) PMID: 19204208
114. Lalloo F, et al. Lancet (2003) PMID: 12672316
115. Mandelker D, et al. Ann. Oncol. (2019) PMID: 31050713
116. Jaiswal S, et al. N. Engl. J. Med. (2014) PMID: 25426837
117. Genovese G, et al. N. Engl. J. Med. (2014) PMID: 25426838
118. Xie M, et al. Nat. Med. (2014) PMID: 25326804
119. Acuna-Hidalgo R, et al. Am. J. Hum. Genet. (2017) PMID: 28669404
120. Severson EA, et al. Blood (2018) PMID: 29678827
121. Fuster JJ, et al. Circ. Res. (2018) PMID: 29420212
122. Hematology Am Soc Hematol Educ Program (2018) PMID: 30504320
123. Chabon JJ, et al. Nature (2020) PMID: 32269342
124. Razavi P, et al. Nat. Med. (2019) PMID: 31768066

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by J. Keith Killian, M.D. | 07 February 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. · 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531