

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 Soft tissue spindle cell lipoma	PHYSICIAN	ORDERING PHYSICIAN Yeh, Yi-Chen	SPECIMEN	SPECIMEN ID CCF 8/29/1968
	NAME Fang, Chuan-Chuan		MEDICAL FACILITY Taipei Veterans General Hospital		SPECIMEN TYPE Blood
	DATE OF BIRTH 29 August 1968		ADDITIONAL RECIPIENT None		DATE OF COLLECTION 28 November 2022
	SEX Female		MEDICAL FACILITY ID 205872		SPECIMEN RECEIVED 01 December 2022
	MEDICAL RECORD # 33525018		PATHOLOGIST Not Provided		

Biomarker Findings

Blood Tumor Mutational Burden - 5 Muts/Mb
Microsatellite status - MSI-High Not Detected
Tumor Fraction - Elevated Tumor Fraction

Genomic Findings

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

DNMT3A V675fs*29
NF1R2583fs*12
PTCH1I941fs*18

Report Highlights

- Variants that may represent clonal hematopoiesis and may originate from non-tumor sources: **DNMT3A V675fs*29** (p. 5)

BIOMARKER FINDINGS

Blood Tumor Mutational Burden -
 5 Muts/Mb

Microsatellite status -
 MSI-High Not Detected

Tumor Fraction -
 Elevated Tumor Fraction

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. There is higher sensitivity for identifying genomic alterations and a lower risk of false negative results in specimens with elevated tumor fraction; the positive percent agreement observed between liquid and tissue for defined short variants is $\geq 90\%$ (Li et al., 2021; AACR Abstract 2231) (see Biomarker Findings section).

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

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<https://www.rochefoundationmedicine.com/home/contact-us.html>

VARIANTS THAT MAY REPRESENT CLONAL HEMATOPOIESIS (CH)

Genomic findings below may include nontumor somatic alterations, such as CH. The efficacy of targeting such nontumor somatic alterations is unknown. This content should be interpreted based on clinical context. Refer to appendix for additional information on CH.

DNMT3A - V675fs*29 p. 5

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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.

DNMT3A - V675fs*29 **p. 5** **PTCH1 - I941fs*18** **p. 6**
NF1 - R2583fs*12 **p. 5**

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.

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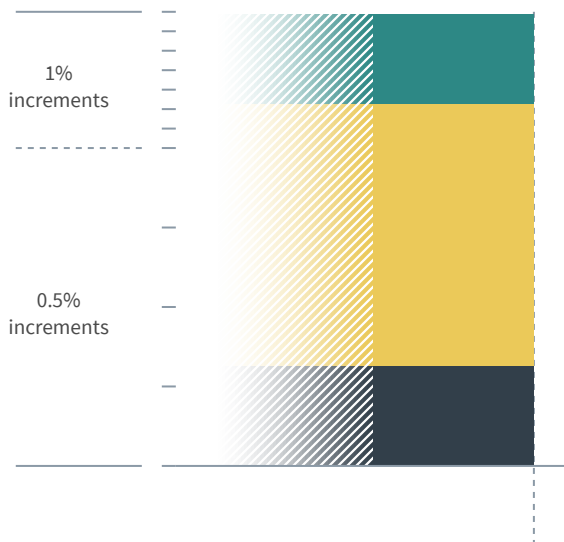
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ORDERED TEST # ORD-1514792-01

Variant Allele
Frequency Percentage
(VAF%)



FoundationOne®Liquid CDx
12 Dec 2022

HISTORIC PATIENT FINDINGS

ORD-1514792-01
VAF%

Blood Tumor Mutational Burden

5 Muts/Mb

Microsatellite status

MSI-High Not Detected

Tumor Fraction

13%

DNMT3A

● V675fs*29

0.63%

NF1

● R2583fs*12

4.6%

PTCH1

● I941fs*18

3.7%

NOTE This comparison table refers only to genes and biomarkers assayed by prior FoundationOne®Liquid CDx 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

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BIOMARKER FINDINGS

BIOMARKER

Blood Tumor Mutational Burden

RESULT

5 Muts/Mb

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

On the basis of clinical evidence in solid tumors, increased blood tumor mutational burden (bTMB) may be associated with greater sensitivity to immunotherapeutic agents, including anti-PD-L1¹⁻³, anti-PD-1³⁻⁴, anti-PD-1/CTLA4 therapies⁵⁻⁶, anti-PD-L1/CTLA4 therapies⁷⁻¹⁰. A Phase 2 multi-solid-tumor trial showed that bTMB ≥ 16 Muts/Mb (as measured by this assay) was associated with improved survival from treatment with a PD-1 inhibitor alone or in combination with a CTLA-4 inhibitor⁵. In non-small cell lung cancer (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 Muts/Mb-16 Muts/Mb^{1,8-10}. In head and neck squamous cell carcinoma (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 inhibitor¹¹. In colorectal cancer (CRC), a Phase 2 study showed that bTMB ≥ 28 Muts/Mb (approximate equivalency ≥ 14 Muts/Mb as measured by this assay) was associated with improved OS from a PD-L1 inhibitor alone or in combination with a CTLA-4 inhibitor⁷. It is not known whether any targeted therapeutic approach would be relevant in the context of non-malignant conditions, as observed here.

FREQUENCY & PROGNOSIS

Average bTMB levels in solid tumors other than NSCLC have not been evaluated (PubMed, Mar 2022). Published data investigating the prognostic implications of bTMB levels in sarcoma are limited (PubMed, Jul 2022). Published data investigating the prognostic implications of tissue TMB in sarcoma are conflicting (PubMed, Feb 2022). High tissue TMB was associated with improved PFS and metastasis-free survival in a study of

undifferentiated sarcomas¹², but with reduced survival in a study of patients with rhabdomyosarcoma¹³.

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 melanoma¹⁴⁻¹⁵ and cigarette smoke in lung cancer¹⁶⁻¹⁷, treatment with temozolomide-based chemotherapy in glioma¹⁸⁻¹⁹, mutations in the proofreading domains of DNA polymerases encoded by the POLE and POLD1 genes²⁰⁻²⁴, and microsatellite instability (MSI)^{20,23-24}. 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 agents¹⁻²⁴. 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

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

Specimens with elevated tumor fraction 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. 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 management²⁵⁻³⁰. It is not known whether any targeted therapeutic approach would be relevant in the context of non-malignant conditions, as observed here.

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)³¹. Elevated tumor fraction levels have been reported to be associated with worse prognosis in a variety of cancer types, including pancreatic cancer³², Ewing sarcoma and osteosarcoma³³, prostate cancer²⁸, breast cancer³⁴, leiomyosarcoma³⁵, esophageal cancer³⁶, colorectal cancer³⁷, and gastrointestinal cancer³⁸.

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 content³⁹, 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 therapy⁴⁰⁻⁴¹.

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ORDERED TEST # ORD-1514792-01

GENOMIC FINDINGS

GENE

DNMT3A

ALTERATION

V675fs*29

TRANSCRIPT ID

NM_022552.3

CODING SEQUENCE EFFECT

2023_2027GTGCG>T

VARIANT CHROMOSOMAL POSITION

chr2:25464486-25464490

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no targeted therapies available to address genomic alterations in DNMT3A in solid tumors. It is not known whether any targeted therapeutic approach would be relevant in the context of non-malignant conditions, as observed here.

FREQUENCY & PROGNOSIS

DNMT3A alterations have been reported at relatively low frequencies in solid tumors and are more prevalent in hematological malignancies (cBioPortal, Feb 2022)⁴²⁻⁴³. Published data investigating the prognostic implications of DNMT3A alterations in solid tumors are limited (PubMed, Feb 2022).

FINDING SUMMARY

The DNMT3A gene encodes the protein DNA methyltransferase 3A, an enzyme that is involved in the methylation of newly synthesized DNA, a function critical for gene regulation⁴⁴⁻⁴⁵. The role of DNMT3A in cancer is uncertain, as some reports describe increased expression and contribution to tumor growth, whereas others propose a role for DNMT3A as a tumor suppressor⁴⁶⁻⁵¹. Alterations such as seen here may disrupt DNMT3A function or expression⁵²⁻⁵⁵.

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 expansion⁵⁶⁻⁶¹. CH in this gene has been associated with increased mortality, risk of coronary heart disease, risk of ischemic stroke, and risk of secondary hematologic malignancy⁵⁶⁻⁵⁷. Clinical management of patients with CH in this gene may include monitoring for hematologic changes and reduction of controllable risk factors for cardiovascular disease⁶². Comprehensive genomic profiling of solid tumors detects nontumor alterations that are due to CH^{60,63-64}. Patient-matched peripheral blood mononuclear cell sequencing is required to conclusively determine if this alteration is present in tumor or is secondary to CH.

GENE

NF1

ALTERATION

R2583fs*12

TRANSCRIPT ID

NM_001042492.2

CODING SEQUENCE EFFECT

7747_7748delAG

VARIANT CHROMOSOMAL POSITION

chr17:29683983-29683985

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

On the basis of clinical evidence in neurofibromatosis Type 1-associated neurofibroma⁶⁵⁻⁶⁸, glioma or glioblastoma⁶⁸⁻⁷², and non-small cell lung cancer⁷³, NF1 inactivation may predict sensitivity to MEK inhibitors such as cobimetinib, trametinib, binimetinib, and selumetinib. On the basis of limited clinical data⁷⁴⁻⁷⁶ and preclinical data⁷⁷⁻⁷⁸, loss or inactivation of NF1 may predict sensitivity to mTOR inhibitors, including everolimus and temsirolimus. A preclinical study suggests that combined mTOR and MEK inhibition is effective

in a model of NF1-deficient malignant peripheral nerve sheath tumors (MPNST)⁷⁹. 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. It is not known whether any targeted therapeutic approach would be relevant in the context of non-malignant conditions, as observed here.

FREQUENCY & PROGNOSIS

NF1 alterations are common in various solid tumors, with mutations being more frequent than gene loss, and are often seen in melanoma (18%), glioma (14%), gastrointestinal stromal tumor (GIST; 10%), and in salivary gland (6.1%), ovarian (5.4%), breast (4.8%), non-small cell lung (4.7%), non-melanoma skin (4.7%), and endometrial (3.7%) cancer⁸⁰. There are rare reports of leiomyosarcoma arising in patients with neurofibromatosis with the assumption of NF1 mutation⁸¹⁻⁸². The appearance of soft tissue sarcoma in patients with neurofibromatosis is associated with a poor prognosis⁸³.

FINDING SUMMARY

NF1 encodes neurofibromin, a GTPase-activating protein (GAP) that is a key negative regulator of the RAS signaling pathway⁸⁴. Neurofibromin acts as a

tumor suppressor by repressing RAS signaling⁸⁵. The consequences of alterations that may leave the GAP-related domain intact, such as seen here, are unclear; however, similar alterations have been previously reported in the context of cancer, which may indicate biological relevance.

POTENTIAL GERMLINE IMPLICATIONS

One or more of the NF1 variants observed here has been described in the ClinVar database as a likely pathogenic or pathogenic germline mutation (by an expert panel or multiple submitters) associated with neurofibromatosis type 1 (ClinVar, Sep 2022)⁸⁶. Follow-up germline testing would be needed to distinguish whether the finding in this patient is somatic or germline. Germline mutations in NF1 cause the autosomal dominant disorder neurofibromatosis type 1, which is characterized in part by increased risk of developing various tumors, including sarcoma, glioma, breast carcinoma, and neuroendocrine and hematological neoplasms⁸⁷⁻⁸⁹. Estimates for the prevalence of the disorder in the general population range from 1:2,500 to 1:3,000⁹⁰⁻⁹¹, and in the appropriate clinical context, germline testing of NF1 is recommended.

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GENOMIC FINDINGS
GENE

PTCH1

ALTERATION

I941fs*18

TRANSCRIPT ID

NM_000264.3

CODING SEQUENCE EFFECT

2821_2822insA

VARIANT CHROMOSOMAL POSITION

chr9:98221947

CR, 5/8 PR)⁹⁶ and medulloblastoma (DCR 70%, 7/10)⁹⁸. In other tumor types, the efficacy of vismodegib and sonidegib is more limited. In a basket trial, 17% (3/18) of patients with PTCH1-mutated tumors achieved a PR from vismodegib¹⁰¹. An additional basket trial reported all 6 patients with PTCH1 alterations experienced PD from sonidegib¹⁰². It is not known whether any targeted therapeutic approach would be relevant in the context of non-malignant conditions, as observed here.

12-transmembrane protein that functions as an inhibitor of Smoothened (SMO) and downstream Hedgehog (Hh) signaling¹⁰⁴. PTCH1 is a receptor for Hh ligands¹⁰⁵ and Hh ligand binding to PTCH1 results in derepression of SMO and downstream activation GLI-family transcription factors¹⁰⁶. Inactivating germline mutations in PTCH1 are associated with Basal Cell Nevus Syndrome (Gorlin syndrome)¹⁰⁷⁻¹⁰⁸. Patients with Gorlin syndrome develop basal cell carcinomas and are also predisposed to medulloblastoma. Somatic mutations that inactivate PTCH1 are frequently found in the sporadic forms of these cancers. Alterations such as seen here may disrupt PTCH1 function or expression. PTCH1 alterations including characterized loss of function mutations¹⁰⁹⁻¹¹⁰, or alterations that are associated with Gorlin syndrome¹¹¹ or Sonic Hedgehog subgroup medulloblastoma¹¹²⁻¹¹⁴, are predicted to result in increased Hedgehog signaling; patients with PTCH1 mutations have had significant clinical responses to SMO inhibitors⁹⁶⁻⁹⁷.

FREQUENCY & PROGNOSIS

Inactivating PTCH1 alterations are rare in sarcoma and have been reported in 2% (1/50) of the dedifferentiated liposarcomas analyzed in the MSKCC sarcoma dataset¹⁰³. Published data investigating the prognostic implications of PTCH1 alteration in liposarcoma are limited (PubMed, Dec 2022).

FINDING SUMMARY

The PTCH1 tumor suppressor gene encodes a

POTENTIAL TREATMENT STRATEGIES
— Targeted Therapies —

Activation of SMO or loss of PTCH1 can result in activation of downstream Hedgehog signaling (Hh)⁹²⁻⁹⁵ and may predict sensitivity to SMO inhibitors such as vismodegib⁹⁶⁻⁹⁹ and sonidegib¹⁰⁰. Clinical responses to vismodegib have been reported for patients with PTCH1-mutated basal cell carcinoma (BCC) (1/8

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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.

ALK
 G743V

CARD11
 A209T

DOT1L
 A438T

FAM123B
 D919A

FANCA
 rearrangement

KDM5A
 A1361T

MED12
 I2047V

NF2
 R462H

NOTCH1
 Q1134R

NOTCH3
 A1450T

PTCH1
 R1342H

RARA
 T285A

ROS1
 S2255L

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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 or WTX)	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	BTB Exons 2, 15	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	EMSY (C11orf30)	EP300	EPHA3
EPHB1	EPHB4	ERBB2	ERBB3 Exons 3, 6, 7, 8, 10, 12, 20, 21, 23, 24, 25	ERBB4	ERCC4	ERG	ERRF1	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	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	GID4 (C17orf39)	GNA11 Exons 4, 5
GNA13	GNAQ Exons 4, 5	GNAS Exons 1, 8	GRM3	GSK3B	H3-3A (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)	KRAS

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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.

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	MRE11 (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
NSD2 (WHSC1 or MMSET)	NSD3 (WHSC1L1)	NT5C2	NTRK1 Exons 14, 15, Introns 8-11	NTRK2 Intron 12	NTRK3 Exons 16, 17	NUTM1* Intron 1	P2RY8	PALB2
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)	PIK3CB	PIK3R1	PIM1	PMS2	POLD1
POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI	PRKN (PARK2)	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	SOCS1	SOX2	SOX9	SPEN	SPOP	SRC	STAG2
STAT3	STK11	SUFU	SYK	TBX3	TEK	TENT5C (FAM46C)	TERC* ncRNA	TERT* Promoter
TET2	TGFBR2	TIPARP	TMPRSS2* Introns 1-3	TNFAIP3	TNFRSF14	TP53	TSC1	TSC2
TYRO3	U2AF1	VEGFA	VHL	WT1	XPO1	XRCC2	ZNF217	ZNF703

ADDITIONAL ASSAYS: FOR THE DETECTION OF SELECT CANCER BIOMARKERS

Microsatellite (MS) status
Blood Tumor Mutational Burden (bTMB)
Tumor Fraction

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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, Ciplastraat 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 to: *ASXL1*, *ATM*, *CBL*, *CHEK2*, *DNMT3A*, *JAK2*,

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About FoundationOne® Liquid CDx

KMT2D (MLL2), MPL, MYD88, SF3B1, TET2, TP53, and U2AF1.

- 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.
- 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. 2022. 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.

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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

REFERENCE SEQUENCE INFORMATION

Sequence data is mapped to the human genome, Genome Reference Consortium Human Build 37 (GRCh37), also known as hg19.

MR Suite Version (RG) 7.4.0

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References

1. Gandara DR, et al. *Nat. Med.* (2018) PMID: 30082870
2. Wang Z, et al. *JAMA Oncol* (2019) PMID: 30816954
3. Sturgill EG, et al. *Oncologist* (2022) PMID: 35274716
4. Aggarwal C, et al. *Clin. Cancer Res.* (2020) PMID: 32102950
5. Schenker et al., 2022; AACR Abstract CT022
6. Saori et al., 2021; ESMO Abstract 80P
7. Chen EX, et al. *JAMA Oncol* (2020) PMID: 32379280
8. Rizvi NA, et al. *JAMA Oncol* (2020) PMID: 32271377
9. Si H, et al. *Clin. Cancer Res.* (2021) PMID: 33355200
10. Leighl NB, et al. *J Thorac Oncol* (2022) PMID: 34800700
11. Li et al., 2020; ASCO Abstract 6511
12. Steele CD, et al. *Cancer Cell* (2019) PMID: 30889380
13. Casey DL, et al. *Clin. Cancer Res.* (2020) PMID: 31699828
14. Pfeifer GP, et al. *Mutat. Res.* (2005) PMID: 15748635
15. Hill VK, et al. *Annu Rev Genomics Hum Genet* (2013) PMID: 23875803
16. Pfeifer GP, et al. *Oncogene* (2002) PMID: 12379884
17. Rizvi NA, et al. *Science* (2015) PMID: 25765070
18. Johnson BE, et al. *Science* (2014) PMID: 24336570
19. Choi S, et al. *Neuro-oncology* (2018) PMID: 29452419
20. Cancer Genome Atlas Research Network, et al. *Nature* (2013) PMID: 23636398
21. Briggs S, et al. *J. Pathol.* (2013) PMID: 23447401
22. Heitzer E, et al. *Curr. Opin. Genet. Dev.* (2014) PMID: 24583393
23. *Nature* (2012) PMID: 22810696
24. Roberts SA, et al. *Nat. Rev. Cancer* (2014) PMID: 25568919
25. Bronkhorst AJ, et al. *Biomol Detect Quantif* (2019) PMID: 30923679
26. Raja R, et al. *Clin. Cancer Res.* (2018) PMID: 30093454
27. Hrebien S, et al. *Ann. Oncol.* (2019) PMID: 30860573
28. Choudhury AD, et al. *JCI Insight* (2018) PMID: 30385733
29. Goodall J, et al. *Cancer Discov* (2017) PMID: 28450425
30. Goldberg SB, et al. *Clin. Cancer Res.* (2018) PMID: 29330207
31. Bettgeowda C, et al. *Sci Transl Med* (2014) PMID: 24553385
32. Lapin M, et al. *J Transl Med* (2018) PMID: 30400802
33. Shulman DS, et al. *Br. J. Cancer* (2018) PMID: 30131550
34. Stover DG, et al. *J. Clin. Oncol.* (2018) PMID: 29298117
35. Hemming ML, et al. *JCO Precis Oncol* (2019) PMID: 30793095
36. Egyud M, et al. *Ann. Thorac. Surg.* (2019) PMID: 31059681
37. Fan G, et al. *PLoS ONE* (2017) PMID: 28187169
38. Vu et al., 2020; DOI: 10.1200/PO.19.00204
39. Li G, et al. *J Gastrointest Oncol* (2019) PMID: 31602320
40. Zhang EW, et al. *Cancer* (2020) PMID: 32757294
41. Butler TM, et al. *Cold Spring Harb Mol Case Stud* (2019) PMID: 30833418
42. Cerami E, et al. *Cancer Discov* (2012) PMID: 22588877
43. Gao J, et al. *Sci Signal* (2013) PMID: 23550210
44. Trowbridge JJ, et al. *Nat. Genet.* (2011) PMID: 22200773
45. *Prog Mol Biol Transl Sci* (2011) PMID: 21507354
46. Yang J, et al. *Mol Med Rep* () PMID: 21887466
47. Vallböhmer D, et al. *Clin Lung Cancer* (2006) PMID: 16870044
48. Daskalos A, et al. *Cancer* (2011) PMID: 21351083
49. Fabbri M, et al. *Proc. Natl. Acad. Sci. U.S.A.* (2007) PMID: 17890317
50. Gao Q, et al. *Proc. Natl. Acad. Sci. U.S.A.* (2011) PMID: 22011581
51. Kim MS, et al. *APMIS* (2013) PMID: 23031157
52. Chen ZX, et al. *J. Cell. Biochem.* (2005) PMID: 15861382
53. Guo X, et al. *Nature* (2015) PMID: 25383530
54. Sandoval JE, et al. *J. Biol. Chem.* (2019) PMID: 30705090
55. Zhang ZM, et al. *Nature* (2018) PMID: 29414941
56. Jaiswal S, et al. *N. Engl. J. Med.* (2014) PMID: 25426837
57. Genovese G, et al. *N. Engl. J. Med.* (2014) PMID: 25426838
58. Xie M, et al. *Nat. Med.* (2014) PMID: 25326804
59. Acuna-Hidalgo R, et al. *Am. J. Hum. Genet.* (2017) PMID: 28669404
60. Severson EA, et al. *Blood* (2018) PMID: 29678827
61. Fuster JJ, et al. *Circ. Res.* (2018) PMID: 29420212
62. *Hematology Am Soc Hematol Educ Program* (2018) PMID: 30504320
63. Chabon JJ, et al. *Nature* (2020) PMID: 32269342
64. Razavi P, et al. *Nat. Med.* (2019) PMID: 31768066
65. Dombi E, et al. *N. Engl. J. Med.* (2016) PMID: 28029918
66. Schalkwijk S, et al. *Cancer Chemother Pharmacol* (2021) PMID: 33903938
67. Toledano H, et al. *Childs Nerv Syst* (2021) PMID: 33751171
68. Ronsley R, et al. *Cancer Med* (2021) PMID: 33939292
69. Fangusaro J, et al. *Lancet Oncol.* (2019) PMID: 31151904
70. Manoharan N, et al. *J Neurooncol* (2020) PMID: 32780261
71. Kondyli M, et al. *J Neurooncol* (2018) PMID: 30097824
72. Awada G, et al. *Case Rep Oncol* () PMID: 33082744
73. Middleton G, et al. *Nature* (2020) PMID: 32669708
74. Lim SM, et al. *Oncotarget* (2016) PMID: 26859683
75. Weiss B, et al. *Neuro-oncology* (2015) PMID: 25314964
76. Janku F, et al. *Oncotarget* (2014) PMID: 24931142
77. Johannessen CM, et al. *Curr. Biol.* (2008) PMID: 18164202
78. Johannessen CM, et al. *Proc. Natl. Acad. Sci. U.S.A.* (2005) PMID: 15937108
79. Malone CF, et al. *Cancer Discov* (2014) PMID: 24913553
80. Zehir A, et al. *Nat. Med.* (2017) PMID: 28481359
81. Liew MA, et al. *Pediatr. Dev. Pathol. ()* PMID: 11910511
82. Kluger N, et al. *Cases J* (2009) PMID: 19946501
83. Bień E, et al. *Med Wieku Rozwoj* () PMID: 18663267
84. Hattori S, et al. *Biochem. Biophys. Res. Commun.* (1991) PMID: 1904223
85. Morcos P, et al. *Mol. Cell. Biol.* (1996) PMID: 8628317
86. Landrum MJ, et al. *Nucleic Acids Res.* (2018) PMID: 29165669
87. Jett K, et al. *Genet. Med.* (2010) PMID: 20027112
88. Patil S, et al. *Oncologist* (2012) PMID: 22240541
89. Evans DG, et al. *Clin Sarcoma Res* (2012) PMID: 23036231
90. Upadhyaya M, et al. *J. Med. Genet.* (1995) PMID: 8544190
91. Williams VC, et al. *Pediatrics* (2009) PMID: 19117870
92. Shou Y, et al. *Clin. Cancer Res.* (2015) PMID: 25473003
93. Rodon J, et al. *Clin. Cancer Res.* (2014) PMID: 24523439
94. Migden MR, et al. *Lancet Oncol.* (2015) PMID: 25981810
95. Kieran MW, et al. *Neuro Oncol* (2017) PMID: 28605510
96. Von Hoff DD, et al. *N. Engl. J. Med.* (2009) PMID: 19726763
97. Rudin CM, et al. *N. Engl. J. Med.* (2009) PMID: 19726761
98. Robinson GW, et al. *J. Clin. Oncol.* (2015) PMID: 26169613
99. Frappaz D, et al. *Neuro Oncol* (2021) PMID: 33825892
100. Lear JT, et al. *Clin Cosmet Investig Dermatol* (2020) PMID: 32104037
101. Hainsworth JD, et al. *J. Clin. Oncol.* (2018) PMID: 29320312
102. Slosberg ED, et al. *Oncotarget* (2018) PMID: 29765547
103. Barretina J, et al. *Nat. Genet.* (2010) PMID: 20601955
104. Taipale J, et al. *Nature* (2002) PMID: 12192414
105. Stone DM, et al. *Nature* (1996) PMID: 8906787
106. Stanton BZ, et al. *Mol Biosyst* (2010) PMID: 20024066
107. Johnson RL, et al. *Science* (1996) PMID: 8658145
108. Hahn H, et al. *Cell* (1996) PMID: 8681379
109. Yauch RL, et al. *Science* (2009) PMID: 19726788
110. Chung JH, et al. *Oncotarget* (2013) PMID: 24368541
111. Sharpe HJ, et al. *Cancer Cell* (2015) PMID: 25759019
112. Kool M, et al. *Cancer Cell* (2014) PMID: 24651015
113. Pugh TJ, et al. *Nature* (2012) PMID: 22820256
114. Jones DT, et al. *Nature* (2012) PMID: 22832583

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