

Patient Name: 윤성일  
Gender: M  
Sample ID: N25-315

Primary Tumor Site: Thyroid  
Collection Date: 2023.01.13.

## Sample Cancer Type: Thyroid Cancer

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## Relevant Thyroid Cancer Findings

Gene	Finding
BRAF	<b>BRAF p.(V600E) c.1799T&gt;A</b>
NTRK1	None detected
NTRK2	None detected
NTRK3	None detected
RET	None detected

Genomic Alteration	Finding
Tumor Mutational Burden	<b>3.79 Mut/Mb measured</b>

## Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	<b>BRAF p.(V600E) c.1799T&gt;A</b> B-Raf proto-oncogene, serine/threonine kinase Allele Frequency: 35.10% Locus: chr7:140453136 Transcript: NM_004333.6	<b>dabrafenib + trametinib</b> <sup>1 / II+</sup> dabrafenib vemurafenib	<b>binimetinib + encorafenib</b> <sup>1, 2 / I, II+</sup> <b>cetuximab + encorafenib</b> <sup>1, 2 / I, II+</sup> <b>cetuximab + encorafenib + chemotherapy</b> <sup>1 / I, II+</sup> <b>cobimetinib + vemurafenib</b> <sup>1, 2 / I, II+</sup> <b>dabrafenib</b> <sup>1, 2 / I, II+</sup> <b>dabrafenib + trametinib</b> <sup>1, 2 / I, II+</sup> <b>vemurafenib</b> <sup>1, 2 / I, II+</sup> <b>atezolizumab + cobimetinib + vemurafenib</b> <sup>1 / II+</sup> <b>trametinib</b> <sup>1, 2</sup> encorafenib <sup>I, II+</sup> encorafenib + panitumumab <sup>I, II+</sup> encorafenib + panitumumab + chemotherapy <sup>I, II+</sup> ipilimumab + nivolumab <sup>I, II+</sup> bevacizumab + chemotherapy <sup>I</sup>	23

\* Public data sources included in relevant therapies: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, ESMO

\* Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

Line of therapy: I: First-line therapy, II+: Other line of therapy


Tier Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.

Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
			anti-PD-1 <sup>II+</sup> dabrafenib + pembrolizumab + trametinib <sup>II+</sup> ipilimumab <sup>II+</sup> nivolumab <sup>II+</sup> nivolumab + relatlimab <sup>II+</sup> pembrolizumab <sup>II+</sup> dabrafenib + MEK inhibitor selumetinib tovorafenib	
IIC	TERT c.-124C>T telomerase reverse transcriptase Allele Frequency: 43.61% Locus: chr5:1295228 Transcript: NM_198253.3	None*	None*	1

\* Public data sources included in relevant therapies: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, ESMO  
\* Public data sources included in prognostic and diagnostic significance: NCCN, ESMO  
Line of therapy: I: First-line therapy, II+: Other line of therapy  
Tier Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.

 Alerts informed by public data sources:  Contraindicated,  Resistance,  Breakthrough,  Fast Track

BRAF p.(V600E) c.1799T>A  plixorafenib <sup>1</sup>

Public data sources included in alerts: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources  
HLA-A p.(L180\*) c.539T>A, ARID5B deletion, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden

Variant Details

DNA Sequence Variants							
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
BRAF	p.(V600E)	c.1799T>A	COSM476	chr7:140453136	35.10%	NM_004333.6	missense
TERT	p.(?)	c.-124C>T	VCV001299388	chr5:1295228	43.61%	NM_198253.3	unknown
HLA-A	p.(L180*)	c.539T>A	.	chr6:29911240	65.46%	NM_001242758.1	nonsense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	46.28%	NM_000903.3	missense
CHIA	p.(I338=;I339V)	c.1014_1015delCAinsT G	.	chr1:111861840	2.33%	NM_201653.4	synonymous, missense
FAT1	p.(G2036S)	c.6106G>A	.	chr4:187541634	3.51%	NM_005245.4	missense
ARID1B	p.(G408E)	c.1223G>A	.	chr6:157100037	4.09%	NM_001371656.1	missense
PTCH1	p.(R13G)	c.37C>G	.	chr9:98270607	66.71%	NM_000264.5	missense
CD163	p.(S1050F)	c.3149C>T	.	chr12:7635337	2.29%	NM_004244.5	missense
CD276	p.(A312V)	c.935C>T	.	chr15:73996201	14.46%	NM_001024736.2	missense
NF1	p.(I342V)	c.1024A>G	.	chr17:29527575	9.22%	NM_001042492.3	missense
NF1	p.(V1042I)	c.3124G>A	.	chr17:29557870	3.21%	NM_001042492.3	missense

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
DSC1	p.(T341I)	c.1022C>T	.	chr18:28723672	2.85%	NM_024421.2	missense
ZNF831	p.(D1515N)	c.4543G>A	.	chr20:57829307	49.70%	NM_178457.3	missense
KDM5C	p.(P144S)	c.430C>T	.	chrX:53247070	3.24%	NM_004187.5	missense
ATRX	p.(D1468N)	c.4402G>A	.	chrX:76907759	3.39%	NM_000489.6	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
ARID5B	chr10:63661463	0.69	0.66

Biomarker Descriptions

BRAF p.(V600E) c.1799T>A

B-Raf proto-oncogene, serine/threonine kinase

Background: The BRAF gene encodes the B-Raf proto-oncogene serine/threonine kinase, a member of the RAF family of serine/threonine protein kinases which also includes ARAF and RAF1(CRAF)<sup>17</sup>. BRAF is among the most commonly mutated kinases in cancer. Activation of the MAPK pathway occurs through BRAF mutations and leads to an increase in cell division, dedifferentiation, and survival<sup>18,19</sup>. BRAF mutations are categorized into three distinct functional classes, namely, class 1, 2, and 3, and are defined by the dependency on the RAS pathway<sup>20</sup>. Class 1 and 2 BRAF mutants are RAS-independent in that they signal as active monomers (Class 1) or dimers (Class 2) and become uncoupled from RAS GTPase signaling, resulting in constitutive activation of BRAF<sup>20</sup>. Class 3 mutants are RAS dependent as the kinase domain function is impaired or dead<sup>20,21,22</sup>.

Alterations and prevalence: Somatic mutations in BRAF are observed in 59% of thyroid carcinoma, 53% of skin cutaneous melanoma, 12% of colorectal adenocarcinoma, 8% of lung adenocarcinoma, 5% of uterine corpus endometrial carcinoma, and 2-3% of bladder urothelial carcinoma, lung squamous cell carcinoma, stomach adenocarcinoma, cholangiocarcinoma, diffuse large B-cell lymphoma, glioblastoma multiforme, uterine carcinosarcoma, and head and neck squamous cell carcinoma<sup>8,9</sup>. Mutations at V600 belong to class 1 and include V600E, the most recurrent somatic BRAF mutation across diverse cancer types<sup>21,23</sup>. Class 2 mutations include K601E/N/T, L597Q/V, G469A/V/R, G464V/E, and BRAF fusions<sup>21</sup>. Class 3 mutations include D287H, V459L, G466V/E/A, S467L, G469E, and N581S/I<sup>21</sup>. BRAF V600E is universally present in hairy cell leukemia, mature B-cell cancers, and prevalent in histiocytic neoplasms<sup>24,25,26</sup>. Other recurrent BRAF somatic mutations cluster in the glycine-rich phosphate-binding loop at codons 464-469 in exon 11, as well as additional codons flanking V600 in the activation loop<sup>23</sup>. BRAF amplification is observed in 8% of ovarian serous cystadenocarcinoma, 4% of skin cutaneous melanoma, and 2% of sarcoma, uterine carcinosarcoma, and glioblastoma multiforme<sup>8,9</sup>. BRAF fusions are mutually exclusive to BRAF V600 mutations and have been described in melanoma, thyroid cancer, pilocytic astrocytoma, NSCLC, and several other cancer types<sup>27,28,29,30,31</sup>. Part of the oncogenic mechanism of BRAF gene fusions is the removal of the N-terminal auto-inhibitory domain, leading to constitutive kinase activation<sup>22,27,29</sup>. Alterations in BRAF are rare in pediatric cancers, with the most predominant being the V600E mutation and the BRAF::KIAA1549 fusion, both of which are observed in low-grade gliomas<sup>32</sup>. Somatic mutations are observed in 6% of glioma and less than 1% of bone cancer (2 in 327 cases), Wilms tumor (1 in 710 cases), and peripheral nervous system cancers (1 in 1158 cases)<sup>8,9</sup>. Amplification of BRAF is observed in 1% or less of Wilms tumor (2 in 136 cases) and B-lymphoblastic leukemia/lymphoma (2 in 731 cases)<sup>8,9</sup>.

Potential relevance: Vemurafenib<sup>33</sup> (2011) is the first targeted therapy approved for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E mutation, and it is also approved for BRAF V600E-positive Erdheim-Chester Disease (2017). BRAF class 1 mutations, including V600E, are sensitive to vemurafenib, whereas class 2 and 3 mutations are insensitive<sup>21</sup>. BRAF kinase inhibitors including dabrafenib<sup>34</sup> (2013) and encorafenib<sup>35</sup> (2018) are also approved for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E/K mutations. Encorafenib<sup>35</sup> is approved in combination with cetuximab<sup>36</sup> (2020) for the treatment of BRAF V600E mutated colorectal cancer. Due to the tight coupling of RAF and MEK signaling, several MEK inhibitors have been approved for patients harboring BRAF alterations<sup>21</sup>. The MEK inhibitors, trametinib<sup>37</sup> (2013) and binimetinib<sup>38</sup> (2018), were approved for the treatment of metastatic melanoma with BRAF V600E/K mutations. Combination therapies of BRAF plus MEK inhibitors have been approved in melanoma and NSCLC<sup>39</sup>. The combinations of dabrafenib/trametinib<sup>37</sup>(2015) and vemurafenib/cobimetinib<sup>40</sup> (2015) were approved for the treatment of patients with unresectable or metastatic melanoma with a

## Biomarker Descriptions (continued)

BRAF V600E/K mutation. Subsequently, the combination of dabrafenib and trametinib was approved for metastatic NSCLC (2017), children with low-grade gliomas, and children and adults with solid tumors (2022) harboring a BRAF V600E mutation<sup>34</sup>. The PD-L1 antibody, atezolizumab<sup>41</sup>, has also been approved in combination with cobimetinib and vemurafenib for BRAF V600 mutation-positive unresectable or metastatic melanoma. The FDA has granted fast track designation (2023) to ABM-1310<sup>42</sup> for BRAF V600E-mutated glioblastoma (GBM) patients. In 2018, binimetinib<sup>43</sup> was also granted breakthrough designation in combination with cetuximab and encorafenib for BRAF V600E mutant metastatic colorectal cancer. The ERK inhibitor ulixertinib<sup>44</sup> was granted fast track designation in 2020 for the treatment of patients with non-colorectal solid tumors harboring BRAF mutations G469A/V, L485W, or L597Q. The FDA granted fast track designation (2022) to the pan-RAF inhibitor, KIN-2787<sup>45</sup>, for the treatment of BRAF class II or III alteration-positive malignant or unresectable melanoma. The FDA also granted fast track designation (2023) to the BRAF inhibitor, plixorafenib (PLX-8394)<sup>46</sup>, for BRAF Class I (V600) and Class II (including fusions) altered cancer patients who have already undergone previous treatments. BRAF fusion is a suggested mechanism of resistance to BRAF targeted therapy in melanoma<sup>47</sup>. Additional mechanisms of resistance to BRAF targeted therapy include BRAF amplification, alternative splice transcripts, as well as activation of PI3K signaling and activating mutations in KRAS, NRAS, and MAP2K1/2 (MEK1/2)<sup>48,49,50,51,52,53,54</sup>. Clinical responses to sorafenib and trametinib in limited case studies of patients with BRAF fusions have been reported<sup>31</sup>.

### TERT c.-124C>T

*telomerase reverse transcriptase*

**Background:** The TERT gene encodes telomerase reverse transcriptase, a component of the telomerase core enzyme along with the internal telomerase RNA template (TERC)<sup>12</sup>. TERT is repressed in most differentiated cells, resulting in telomerase silencing<sup>12</sup>. In cancer, telomerase reactivation is known to contribute to cellular immortalization<sup>12,13</sup>. Increased TERT expression results in telomerase activation, allowing for unlimited cancer cell proliferation through telomere stabilization<sup>12</sup>. In addition to its role in telomere maintenance, TERT has RNA-dependent RNA polymerase activity, which, when deregulated, can promote oncogenesis by facilitating mitotic progression and cancer cell stemness<sup>12</sup>.

**Alterations and prevalence:** Somatic mutations are observed in 4% of skin cutaneous melanoma and uterine corpus endometrial carcinoma, 3% of kidney renal papillary cell carcinoma, and 2% of pancreatic adenocarcinoma, stomach adenocarcinoma, and sarcoma<sup>8,9</sup>. Additionally, TERT promoter mutations causing upregulation are observed in many cancer types, especially non-aural cutaneous melanoma (80% of cases), and glioblastoma (70% of cases)<sup>13</sup>. Specifically, TERT promoter mutations at C228T and C250T are recurrent and result in de novo binding sites for ETS transcription factors, leading to enhanced TERT transcription<sup>12</sup>. Amplification of TERT is observed in 15% of lung squamous cell carcinoma, 14% of esophageal adenocarcinoma, 13% of adrenocortical carcinoma and lung adenocarcinoma, and 10% of bladder urothelial carcinoma, 9% of ovarian serous cystadenocarcinoma, 6% of cervical squamous cell carcinoma, 5% of liver hepatocellular carcinoma, sarcoma, skin cutaneous melanoma, stomach adenocarcinoma, head and neck squamous cell carcinoma, 4% of uterine carcinosarcoma, 3% of uterine corpus endometrial carcinoma, breast invasive carcinoma, and 2% of diffuse large B-cell lymphoma<sup>8,9</sup>. TERT is overexpressed in over 85% of tumors and is considered a universal tumor associated antigen<sup>14</sup>. Alterations in TERT are rare in pediatric cancers<sup>8,9</sup>. Somatic mutations are observed in less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), glioma (2 in 297 cases), bone cancer (1 in 327 cases), and Wilms tumor (1 in 710 cases)<sup>8,9</sup>. TERT amplification is observed in 1-2% of peripheral nervous system cancers (2 in 91 cases), leukemia (2 in 250 cases), and B-lymphoblastic leukemia/lymphoma (5 in 731 cases)<sup>8,9</sup>.

**Potential relevance:** Currently, no therapies are approved for TERT aberrations. TERT promoter mutations are diagnostic of oligodendroglioma IDH-mutant with 1p/19q co-deletion, while the absence of promoter mutations combined with an IDH mutation is characteristic of astrocytoma<sup>15,16</sup>. Due to its immunogenicity and near-universal expression on cancer cells, TERT has been a focus of immunotherapy research, including peptide, dendritic, and DNA vaccines as well as T-cell therapy<sup>14</sup>.

### HLA-A p.(L180\*) c.539T>A

*major histocompatibility complex, class I, A*

**Background:** The HLA-A gene encodes the major histocompatibility complex, class I, A<sup>1</sup>. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells<sup>2</sup>. MHC class I molecules are heterodimers composed of two polypeptide chains,  $\alpha$  and B2M<sup>3</sup>. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the  $\alpha$  polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self<sup>4,5,6</sup>. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-A<sup>7</sup>.

**Alterations and prevalence:** Somatic mutations in HLA-A are observed in 7% of diffuse large B-cell lymphoma (DLBCL), 4% of cervical squamous cell carcinoma and head and neck squamous cell carcinoma, 3% of colorectal adenocarcinoma, and 2% of uterine corpus endometrial carcinoma and stomach adenocarcinoma<sup>8,9</sup>. Biallelic loss of HLA-A is observed in 4% of DLBCL<sup>8,9</sup>.

**Potential relevance:** Currently, no therapies are approved for HLA-A aberrations.

## Biomarker Descriptions (continued)

### ARID5B deletion

#### *AT-rich interaction domain 5B*

**Background:** The ARID5B gene encodes the AT-rich interaction domain 5B protein<sup>1</sup>. ARID5B, also known as MRF2, belongs to the ARID superfamily that also includes ARID1A, ARID1B, and ARID2<sup>10,11</sup>. ARID5B forms a complex with PHF2, which is capable of histone demethylation leading to transcriptional activation of target genes<sup>11</sup>. ARID5B is known to be essential for the development of hematopoietic cells<sup>11</sup>. Several single-nucleotide polymorphisms (SNPs) in ARID5B have been associated with susceptibility of acute lymphoblastic leukemia (ALL)<sup>11</sup>.

**Alterations and prevalence:** Somatic mutations in ARID5B are observed in 15% of uterine corpus endometrial carcinoma, 6% of skin cutaneous melanoma, 5% of diffuse large B-cell lymphoma, 4% of stomach adenocarcinoma<sup>8,9</sup>. Biallelic loss of ARID5B is observed in 1% of kidney chromophobe, lung squamous cell carcinoma, and skin cutaneous melanoma<sup>8,9</sup>.

**Potential relevance:** Currently, no therapies are approved for ARID5B aberrations.

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated    Not recommended    Resistance    Breakthrough    Fast Track

FDA information is current as of 2025-09-17. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

BRAF p.(V600E) c.1799T>A

binimetinib + cetuximab + encorafenib

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

**Supporting Statement:**  
The FDA has granted Breakthrough Therapy designation to the MEK inhibitor, binimetinib, in combination with cetuximab and encorafenib for BRAF V600E mutant metastatic colorectal cancer.

**Reference:**  
<https://markets.businessinsider.com/news/stocks/array-biopharma-receives-fda-breakthrough-therapy-designation-for-braftovi-in-combination-with-mektovi-and-cetuximab-for-brafv600e-mutant-metastatic-colorectal-cancer-1027437791>

plixorafenib

Cancer type: Solid Tumor

Variant class: BRAF V600 mutation

**Supporting Statement:**  
The FDA has granted Fast Track designation to a novel small molecule inhibitor, plixorafenib (PLX-8394), for the treatment of patients with cancers harboring BRAF Class 1 (V600) and Class 2 (including fusions) alterations who have exhausted prior therapies.

**Reference:**  
<https://fore.bio/fore-biotherapeutics-announces-fast-track-designation-granted-by-fda-to-fore8394-for-the-treatment-of-cancers-harboring-braf-class-1-and-class-2-alterations/>

ABM-1310

Cancer type: Glioblastoma IDH-wildtype (Grade 4)

Variant class: BRAF V600E mutation

**Supporting Statement:**  
The FDA has granted Fast Track designation to ABM-1310 for the treatment of glioblastoma (GBM) patients with BRAF V600E mutation.

**Reference:**  
<https://www.prnewswire.com/news-releases/abm-therapeutics-abm-1310-granted-fast-track-designation-by-the-fda-following-orphan-drug-designation-301937168.html>

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4,

## Genes Assayed (continued)

### Genes Assayed for the Detection of DNA Sequence Variants (continued)

IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLC01B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFB1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XPO1, ZNF217, ZNF429

### Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4, ERFF1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, FGF4, FGF9, FGFRL1, FGFRL2, FGFRL3, FGFRL4, FLT3, FLT4, FOXA1, FUBP1, FYN, GATA2, GATA3, GLI3, GNA13, GNAS, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, IDH2, IGF1R, IKBKB, IL7R, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LARP4B, LATS1, LATS2, MAGOH, MAP2K1, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK1, MAPK8, MAX, MCL1, MDM2, MDM4, MECOM, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLH3, MPL, MRE11, MSH2, MSH3, MSH6, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLC01B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFB2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFH3, ZMYM3, ZNF217, ZNF429, ZRSR2

### Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFRL1, FGFRL2, FGFRL3, FGFRL4, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSPO2, RSPO3, TERT

### Genes Assayed with Full Exon Coverage


















































































































































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## Relevant Therapy Summary

 In this cancer type    
  In other cancer type    
  In this cancer type and other cancer types    
  No evidence

### BRAF p.(V600E) c.1799T>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
dabrafenib + trametinib					
dabrafenib					 (II)
vemurafenib					
cobimetinib + vemurafenib					 (II/III)
binimetinib + encorafenib					
cetuximab + encorafenib					
trametinib					
atezolizumab + cobimetinib + vemurafenib					
cetuximab + encorafenib + FOLFOX					
encorafenib					
dabrafenib + pembrolizumab + trametinib					
encorafenib + panitumumab					
encorafenib + panitumumab + FOLFOX					
selumetinib					
tovorafenib					
anti-PD-1					
bevacizumab + CAPOX					
bevacizumab + FOLFOX					
bevacizumab + FOLFOXIRI					
dabrafenib + MEK inhibitor					
ipilimumab					
ipilimumab + nivolumab					
nivolumab					
nivolumab + relatlimab					
pembrolizumab					
dabrafenib, trametinib, cabozantinib					 (III)
trametinib, dabrafenib					 (III)
dabrafenib, trametinib					 (II)
plixorafenib, cobicistat					 (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

 In this cancer type    
  In other cancer type    
  In this cancer type and other cancer types    
  No evidence

### BRAF p.(V600E) c.1799T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
vemurafenib, cobimetinib	×	×	×	×	● (II)
RX208, serplulimab	×	×	×	×	● (I/II)
RX208, trametinib	×	×	×	×	● (I/II)
BDTX-4933	×	×	×	×	● (I)
dabrafenib, trametinib, radiation therapy	×	×	×	×	● (I)
exarafenib, binimetinib	×	×	×	×	● (I)
HSK42360	×	×	×	×	● (I)
JSI-1187	×	×	×	×	● (I)
PF-07799933, cetuximab, binimetinib	×	×	×	×	● (I)
RO-7276389, cobimetinib	×	×	×	×	● (I)
RX208	×	×	×	×	● (I)
ZEN-3694, binimetinib	×	×	×	×	● (I)

### TERT c.-124C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
vemurafenib, cobimetinib	×	×	×	×	● (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Thermo Fisher Scientific's Ion Torrent OncoPrint Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on OncoPrint Reporter (6.1.1 data version 2025.10(006)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from [www.fda.gov](http://www.fda.gov) and is current as of 2025-09-17. NCCN information was sourced from [www.nccn.org](http://www.nccn.org) and is current as of 2025-09-02. EMA information was sourced from [www.ema.europa.eu](http://www.ema.europa.eu) and is current as of 2025-09-17. ESMO information was sourced from [www.esmo.org](http://www.esmo.org) and is current as of 2025-09-02. Clinical Trials information is current as of 2025-09-02. For the most up-to-date information regarding a particular trial, search [www.clinicaltrials.gov](http://www.clinicaltrials.gov) by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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