

Patient Name: 김중순
Gender: Male
Sample ID: N26-26

Primary Tumor Site: Lung
Collection Date: 2026.01.16.

Sample Cancer Type: Lung Cancer

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Relevant Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	KRAS p.(G12D) c.35G>A	ROS1	None detected
MET	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	8.54 Mut/Mb measured

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	KRAS p.(G12D) c.35G>A KRAS proto-oncogene, GTPase Allele Frequency: 63.38% Locus: chr12:25398284 Transcript: NM_033360.4	None*	avutometinib + defactinib ^{1 / II+} bevacizumab + chemotherapy ¹	40

* Public data sources included in relevant therapies: FDA¹, NCCN, EMA², 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.

Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, TP53 p.(Q104*) c.310C>T, YAP1 amplification, UGT1A1 p.(G71R) c.211G>A, TERT amplification, CTNND2 amplification, IKBKB amplification, PDCD1LG2 amplification, 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
KRAS	p.(G12D)	c.35G>A	COSM521	chr12:25398284	63.38%	NM_033360.4	missense
TP53	p.(Q104*)	c.310C>T	.	chr17:7579377	56.71%	NM_000546.6	nonsense
UGT1A1	p.(G71R)	c.211G>A	COSM4415616	chr2:234669144	49.72%	NM_000463.3	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	23.70%	NM_000903.3	missense
PIK3C2B	p.(S1121F)	c.3362C>T	.	chr1:204409337	18.85%	NM_002646.4	missense
OR2L8	p.(G196C)	c.586_588delGGCinsT GT	.	chr1:248112745	1.73%	NM_001001963.1	missense
SETD2	p.(E1984K)	c.5950G>A	.	chr3:47125320	57.57%	NM_014159.7	missense
PABPC4L	p.(L362V)	c.1084C>G	.	chr4:135121091	23.20%	NM_001114734.2	missense
FBXW7	p.(S148T)	c.443G>C	.	chr4:153332513	52.38%	NM_033632.3	missense
CDH10	p.(T708A)	c.2122A>G	.	chr5:24488017	14.71%	NM_006727.5	missense
MSH3	p.(A57_A62del)	c.162_179delTGCAGC GGCCGCAGCGGC	.	chr5:79950707	61.88%	NM_002439.5	nonframeshift Deletion
HLA-B	p.([T118I;L119I])	c.353_355delCCCinsT CA	.	chr6:31324208	100.00%	NM_005514.8	missense, missense
CSMD3	p.(G2253V)	c.6758G>T	.	chr8:113349855	19.14%	NM_198123.2	missense
OR8H2	p.(D12V)	c.35A>T	.	chr11:55872553	30.37%	NM_001005200.1	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
YAP1	chr11:101981594	127.79	33.71
TERT	chr5:1253783	6.54	2.18
CTNND2	chr5:10988230	6.23	2.1
IKBKB	chr8:42129602	5.5	1.91
PDCD1LG2	chr9:5522530	5.25	1.85
SDHA	chr5:218412	7.37	2.39
CDH10	chr5:24487706	7.35	2.39
JAK2	chr9:5021954	5.15	1.82

Biomarker Descriptions

KRAS p.(G12D) c.35G>A

KRAS proto-oncogene, GTPase

Background: The KRAS proto-oncogene encodes a GTPase that functions in signal transduction and is a member of the RAS superfamily which also includes NRAS and HRAS⁷. RAS proteins mediate the transmission of growth signals from the cell surface to the nucleus via the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways, which regulate cell division, differentiation, and survival^{8,9,10}. Germline mutations in KRAS lead to several genetic disorders known as RASopathies, including Noonan syndrome, which results in

Biomarker Descriptions (continued)

heart and congenital defects, growth inhibition, and facial dysmorphic features¹¹. Somatic mutations in KRAS are commonly altered in several cancers including non-small cell lung cancer, pancreatic cancer, and multiple myeloma¹¹.

Alterations and prevalence: The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61^{5,12,13}. Mutations at A59, K117, and A146 have also been observed but are less frequent^{6,14}. Somatic mutations in KRAS are observed in 66% of pancreatic adenocarcinoma, 41% of colorectal adenocarcinoma, 30% of lung adenocarcinoma, 19% of uterine corpus endometrial carcinoma, 12% of uterine carcinosarcoma, 9% of stomach adenocarcinoma, 8% of testicular germ cell tumors, 6% of cholangiocarcinoma, 5% of cervical squamous cell carcinoma, acute myeloid leukemia, and diffuse large B-cell lymphoma, 4% of bladder urothelial carcinoma, and 2% of skin cutaneous melanoma and kidney renal papillary cell carcinoma^{5,6}. KRAS is amplified in 9% of ovarian serous cystadenocarcinoma and testicular germ cell tumors, 8% of stomach adenocarcinoma, 7% of esophageal adenocarcinoma and uterine carcinosarcoma, 6% of lung adenocarcinoma, 4% of pancreatic adenocarcinoma and bladder urothelial carcinoma, 3% of lung squamous cell carcinoma, and 2% of sarcoma, mesothelioma, brain lower grade glioma, and uterine corpus endometrial carcinoma^{5,6}. Alterations in KRAS are also observed in pediatric cancers⁶. Somatic mutations in KRAS are observed in 10% of B-lymphoblastic leukemia/lymphoma (24 in 252 cases), 8% of leukemia (29 in 354 cases), and in less than 1% of embryonal tumors (2 in 332 cases), glioma (1 in 297 cases), Wilms tumor (1 in 710 cases), and peripheral nervous system cancers (1 in 1158 cases)⁶. KRAS is amplified in less than 1% of B-lymphoblastic leukemia/lymphoma (1 in 731 cases)⁶. Structural alterations in KRAS are observed in less than 1% of acute lymphoblastic leukemia (1 in 85 cases)⁶.

Potential relevance: The FDA has approved the small molecule inhibitors, sotorasib¹⁵ (2021) and adagrasib¹⁶ (2022), for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC). Sotorasib and adagrasib are also useful in certain circumstances for KRAS G12C-mutated pancreatic adenocarcinoma¹⁷. The FDA has approved the combination of kinase inhibitors, avutometinib and defactinib¹⁸ (2025), for the treatment of adult patients with KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC) after prior systemic therapy. The FDA has granted breakthrough therapy designation (2022) to the KRAS G12C inhibitor, GDC-6036¹⁹, for KRAS G12C-mutated NSCLC. The KRAS-G12C/NRAS-G12C dual inhibitor, elironrasib²⁰, and the KRAS G12C inhibitor, D3S-001²¹, were both granted breakthrough therapy designation (2025) for KRAS G12C-mutated locally advanced or metastatic NSCLC in adults previously treated with chemotherapy and immunotherapy, excluding KRAS G12C inhibitors. The KRAS-G12C inhibitor, olomorasib²², was granted breakthrough designation (2025) in combination with pembrolizumab²³ for unresectable advanced or metastatic NSCLC with a KRAS G12C mutation and PD-L1 expression \geq 50%. The RAF/MEK clamp, avutometinib²⁴ was also granted fast track designation (2024) in combination with sotorasib for KRAS G12C-mutated metastatic NSCLC in patients who have received at least one prior systemic therapy and have not been previously treated with a KRAS G12C inhibitor. The KRAS G12C inhibitor, BBO-8520²⁵, was granted fast track designation in 2025 for previously treated KRAS G12C-mutated patients with metastatic NSCLC. The RAS inhibitor, daraxonrasib²⁶, was granted breakthrough designation (2025) for previously treated metastatic pancreatic cancer with KRAS G12 mutations. The KRAS G12D (ON/OFF) inhibitor, GFH-375²⁷, was also granted fast track designation (2025) for first-line and previously treated KRAS G12D-mutated locally advanced or metastatic pancreatic adenocarcinoma. The KRAS G12C inhibitor, D3S-001²⁸, was granted fast track designation in 2024 for KRAS G12C-mutated patients with advanced unresectable or metastatic colorectal cancers. The PLK1 inhibitor, onvansertib²⁹, was granted fast track designation (2020) in combination with bevacizumab and FOLFIRI for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). The EGFR antagonists, cetuximab³⁰ and panitumumab³¹, are contraindicated for treatment of colorectal cancer patients with KRAS mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146)¹⁴. Additionally, KRAS mutations are associated with poor prognosis in NSCLC³².

Microsatellite stable

Background: Microsatellites are short tandem repeats (STR) of 1 to 6 bases of DNA between 5 to 50 repeat units in length. There are approximately 0.5 million STRs that occupy 3% of the human genome⁶⁹. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{70,71}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2⁷². Mutations and loss of expression in MMR genes, known as defective MMR (dMMR), lead to MSI. In contrast, when MMR genes lack alterations, they are referred to as MMR proficient (pMMR). Consensus criteria were first described in 1998 and defined MSI-high (MSI-H) as instability in two or more of the following five markers: BAT25, BAT26, D5S346, D2S123, and D17S250⁷³. Tumors with instability in one of the five markers were defined as MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)⁷³. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{74,75,76,77,78}. MSI-H is a hallmark of Lynch syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes⁷¹. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{70,71,75,79}.

Alterations and prevalence: The MSI-H phenotype is observed in 30% of uterine corpus endothelial carcinoma, 20% of stomach adenocarcinoma, 15-20% of colon adenocarcinoma, and 5-10% of rectal adenocarcinoma^{70,71,80,81}. MSI-H is also observed in 5% of adrenal cortical carcinoma and at lower frequencies in other cancers such as esophageal, liver, and ovarian cancers^{80,81}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab²³ (2014) and nivolumab⁸² (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab²³ is also approved

Biomarker Descriptions (continued)

as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR with disease progression on prior therapy who are not candidates for surgery or radiation. Importantly, pembrolizumab is approved for the treatment of MSI-H or dMMR solid tumors that have progressed following treatment, with no alternative option and is the first anti-PD-1 inhibitor to be approved with a tumor agnostic indication²³. Dostarlimab⁸³ (2021) is also approved for dMMR recurrent or advanced endometrial carcinoma or solid tumors that have progressed on prior treatment and is recommended as a subsequent therapy option in dMMR/MSI-H advanced or metastatic colon or rectal cancer^{76,84}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab⁸⁵ (2011), is approved alone or in combination with nivolumab in MSI-H or dMMR colorectal cancer that has progressed following treatment with chemotherapy. MSI-H may confer a favorable prognosis in colorectal cancer although outcomes vary depending on stage and tumor location^{76,86,87}. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients⁸⁷. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H tumors^{88,89}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{88,89}.

TP53 p.(Q104*) c.310C>T

tumor protein p53

Background: The TP53 gene encodes the tumor suppressor protein p53, which binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair⁷. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis⁴³. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential⁴⁴. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers^{45,46}.

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)^{5,6,47,48,49,50}. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common, including substitutions at codons R158, R175, Y220, R248, R273, and R282^{5,6}. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes^{51,52,53,54}. Alterations in TP53 are also observed in pediatric cancers^{5,6}. Somatic mutations are observed in 53% of non-Hodgkin lymphoma, 24% of soft tissue sarcoma, 19% of glioma, 13% of bone cancer, 9% of B-lymphoblastic leukemia/lymphoma, 4% of embryonal tumors, 3% of Wilms tumor and leukemia, 2% of T-lymphoblastic leukemia/lymphoma, and less than 1% of peripheral nervous system cancers (5 in 1158 cases)^{5,6}. Biallelic loss of TP53 is observed in 10% of bone cancer, 2% of Wilms tumor, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and leukemia (1 in 250 cases)^{5,6}.

Potential relevance: The small molecule p53 reactivator, PC14586⁵⁵ (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation^{56,57}. TP53 mutations are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma⁵⁸. TP53 mutations confer poor prognosis and poor risk in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)^{59,60,61,62,63}. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant⁶⁴. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occurring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system⁶⁵.

YAP1 amplification

Yes associated protein 1

Background: The YAP1 gene encodes the Yes1 associated transcriptional regulator⁷. YAP1 functions as a transcriptional coactivator for TEAD transcription factors and is an important effector of the Hippo signaling pathway³³. The Hippo pathway is considered a tumor suppressor pathway due to its involvement in various cellular processes including cell proliferation, apoptosis, stem cell expansion, and negative regulation of YAP1^{33,34}. Aberrations in YAP1, including upregulation, have been associated with tumorigenesis and shorter survival^{34,35}. Germline mutations, specifically R331W, have been associated with an increased risk for lung adenocarcinoma³⁶.

Alterations and prevalence: Somatic mutations in YAP1 are observed in 3% of uterine corpus endometrial carcinoma, 2% of skin cutaneous melanoma, esophageal adenocarcinoma, kidney chromophobe, and 1% of uveal melanoma, kidney renal papillary cell carcinoma, lung squamous cell carcinoma, cervical squamous cell carcinoma, and colorectal adenocarcinoma^{5,6}. Amplification of YAP1 is observed in 10% of cervical squamous cell carcinoma, 5% of head and neck squamous cell carcinoma and ovarian cystadenocarcinoma, and 3% of bladder urothelial carcinoma, sarcoma, and esophageal adenocarcinoma^{5,6}. YAP1 fusions are

Biomarker Descriptions (continued)

observed in 1% of sarcoma, esophageal adenocarcinoma, cervical squamous cell carcinoma, skin cutaneous melanoma, and head and neck squamous cell carcinoma^{5,6}.

Potential relevance: Currently, no therapies are approved for YAP1 aberrations. YAP1::TFE3 fusion is considered an ancillary diagnostic marker for epithelioid hemangioendothelioma³⁷. Overexpression of YAP1 is a poor prognostic marker in hepatocellular carcinoma, gastric cancer, colorectal cancer, non-small cell lung cancer, and small cell lung cancer³³.

UGT1A1 p.(G71R) c.211G>A

UDP glucuronosyltransferase family 1 member A1

Background: The UGT1A1 gene encodes UDP glucuronosyltransferase family 1 member A1, a member of the UDP-glucuronosyltransferase 1A (UGT1A) subfamily of the UGT protein superfamily^{7,93}. UGTs are microsomal membrane-bound enzymes that catalyze the glucuronidation of endogenous and xenobiotic compounds and transform the lipophilic molecules into excretable, hydrophilic metabolites^{93,94}. UGTs play an important role in drug metabolism, detoxification, and metabolite homeostasis. Differential expression of UGTs can promote cancer development, disease progression, as well as drug resistance⁹⁵. Specifically, elevated expression of UGT1As are associated with resistance to many anti-cancer drugs due to drug inactivation and lower active drug concentrations. However, reduced expression and downregulation of UGT1As are implicated in bladder and hepatocellular tumorigenesis and progression due to toxin accumulation^{95,96,97,98}. Furthermore, UGT1A1 polymorphisms, such as UGT1A1*28, UGT1A1*93, and UGT1A1*6, confer an increased risk of severe toxicity to irinotecan-based chemotherapy treatment of solid tumors, due to reduced glucuronidation of the irinotecan metabolite, SN-38⁹⁹.

Alterations and prevalence: Biallelic deletion of UGT1A1 has been observed in 6% of sarcoma, 3% of brain lower grade glioma and uveal melanoma, and 2% of thymoma, cervical squamous cell carcinoma, bladder urothelial carcinoma, head and neck squamous cell carcinoma, and esophageal adenocarcinoma^{5,6}.

Potential relevance: Currently, no therapies are approved for UGT1A1 aberrations.

TERT amplification

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)³⁸. TERT is repressed in most differentiated cells, resulting in telomerase silencing³⁸. In cancer, telomerase reactivation is known to contribute to cellular immortalization^{38,39}. Increased TERT expression results in telomerase activation, allowing for unlimited cancer cell proliferation through telomere stabilization³⁸. 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 stemness³⁸.

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^{5,6}. 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)³⁹. 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 transcription³⁸. 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^{5,6}. TERT is overexpressed in over 85% of tumors and is considered a universal tumor associated antigen⁴⁰. Alterations in TERT are rare in pediatric cancers^{5,6}. 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)^{5,6}. 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)^{5,6}.

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^{41,42}. 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 therapy⁴⁰.

Biomarker Descriptions (continued)

CTNND2 amplification

catenin delta 2

Background: The CTNND2 gene encodes catenin delta 2 protein⁷. CTNND2, also known as NPRAP and δ -catenin, belongs to the delta subfamily of the β -catenin superfamily along with CTNND1⁹⁰. Due to its interaction with the cell junction protein, E-cadherin, CTNND2 overexpression has been observed to disrupt E-cadherin distribution and promote tumor growth^{90,91,92}. Additionally, CTNND2 alteration, particularly overexpression, is observed in several cancer types, supporting an oncogenic role for CTNND2^{90,91,92}.

Alterations and prevalence: Somatic mutations in CTNND2 are observed in 14% of skin cutaneous melanoma, 11% of lung adenocarcinoma, 10% of lung squamous cell carcinoma, 9% of stomach adenocarcinoma and uterine corpus endometrial carcinoma, and 6% of head and neck squamous cell carcinoma, and colorectal adenocarcinoma^{5,6}. Amplification of CTNND2 is observed in 13% of lung squamous cell carcinoma, 10% of lung adenocarcinoma, esophageal adenocarcinoma, and bladder urothelial carcinoma, and 7% of ovarian serous cystadenocarcinoma, sarcoma, adrenocortical adenocarcinoma^{5,6}.

Potential relevance: Currently, no therapies are approved for CTNND2 aberrations.

IKBKB amplification

inhibitor of nuclear factor kappa B kinase subunit beta

Background: The IKBKB gene encodes the nuclear factor kappa B kinase subunit beta, also known as IKK-B. IKBKB is a serine/threonine kinase, which acts as an enzyme protein subunit of the IKK complex¹. IKBKB and IKBKA dimerize to form the regulatory subunit of the IKK complex. Along with modulator IKK γ /NEMO, the IKK complex acts as a master regulator of the family of NF- κ B transcription factors¹. NF- κ B signaling is critical in the inflammatory response and is also known to be implicated in other important physiological processes including cell proliferation². In resting cells, NF- κ B dimers are sequestered in the cytoplasm by I κ B proteins². Upon signal initiation, I κ B proteins are phosphorylated by the IKK complex, leading to I κ B protein degradation and liberation of NF- κ B dimers². Subsequently, released NF- κ B dimers undergo nuclear translocation which leads to the expression of various proinflammatory and cell survival genes^{3,4}.

Alterations and prevalence: Somatic mutations in IKBKB are observed in 6% of uterine carcinoma, 5% of melanoma and diffuse large B-cell lymphoma (DLBCL)^{5,6}. Amplifications are observed in 14% of uterine carcinosarcoma, 7% of breast invasive carcinoma and esophageal cancer^{5,6}. IKBKB activating mutations are most commonly found at lysine 175 and are observed in 8% of splenic marginal B-cell lymphomas¹.

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

PDCD1LG2 amplification

programmed cell death 1 ligand 2

Background: The PDCD1LG2 gene encodes the programmed cell death 1 ligand 2, also known as PD-L2⁷. PDCD1LG2 is a type I transmembrane protein expressed by antigen-presenting cells and tumor cells^{66,67}. PDCD1LG2 is an immunoregulatory ligand of PDCD1, a type I transmembrane inhibitory receptor and immune checkpoint belonging to the CD28/CTLA-4 family within the immunoglobulin superfamily^{66,67}. PDCD1LG2 and CD274 (also known as PD-L1) act as co-inhibitors and regulate immune tolerance of central and peripheral T-cells, reducing proliferation and cytokine production^{66,68}.

Alterations and prevalence: Somatic mutations in PDCD1LG2 are observed in 2% of skin cutaneous melanoma and uterine corpus endometrial carcinoma^{5,6}. Amplifications are observed in 4% of sarcoma, head and neck squamous cell carcinoma, and diffuse large B-cell lymphoma (DLBCL), and 2% of ovarian serous cystadenocarcinoma, esophageal adenocarcinoma, stomach adenocarcinoma, lung squamous cell carcinoma, bladder urothelial carcinoma, uterine carcinosarcoma, and cervical squamous cell carcinoma^{5,6}. Alterations in PDCD1LG2 are rare in pediatric cancers⁶. Somatic mutations in PDCD1LG2 are observed in 3% of pediatric soft tissue sarcoma⁶. Amplification of PDCD1LG2 is observed in 1% of Wilms tumor (2 in 136 cases) and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases)⁶.

Potential relevance: Currently, no therapies are approved for PDCD1LG2 aberrations.

Alerts Informed By Public Data Sources

Current FDA Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

FDA information is current as of 2025-11-25. For the most up-to-date information, search www.fda.gov.

KRAS p.(G12D) c.35G>A

cetuximab

Cancer type: Colorectal Cancer

Label as of: 2021-09-24

Variant class: KRAS G12 mutation

Indications and usage:

Erbix® is an epidermal growth factor receptor (EGFR) antagonist indicated for treatment of:

Head and Neck Cancer

- Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy.
- Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with fluorouracil.
- Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy.

Colorectal Cancer

K-Ras wild-type, EGFR-expressing, metastatic colorectal cancer as determined by FDA-approved test

- in combination with FOLFIRI for first-line treatment,
- in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
- as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

Limitations of Use: Erbix® is not indicated for treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)

- in combination with encorafenib, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125084s279lbl.pdf

KRAS p.(G12D) c.35G>A (continued)

panitumumab

Cancer type: Colorectal Cancer

Label as of: 2025-01-16

Variant class: KRAS G12 mutation

Indications and usage:

VECTIBIX® is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of:

Adult patients with wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test) Metastatic Colorectal Cancer (mCRC)*:

- In combination with FOLFOX for first-line treatment.
- As monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy.

KRAS G12C-mutated Metastatic Colorectal Cancer (mCRC)*

- In combination with sotorasib, for the treatment of adult patients with KRAS G12C-mutated mCRC, as determined by an FDA-approved test, who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

*Limitations of Use: VECTIBIX® is not indicated for the treatment of patients with RAS-mutant mCRC unless used in combination with sotorasib in KRAS G12C-mutated mCRC. VECTIBIX® is not indicated for the treatment of patients with mCRC for whom RAS mutation status is unknown.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125147s213lbl.pdf

daraxonrasib

Cancer type: Pancreatic Cancer

Variant class: KRAS G12 mutation

Supporting Statement:

The FDA has granted Breakthrough designation to the RAS inhibitor, daraxonrasib, for previously treated metastatic pancreatic adenocarcinoma (PDAC) in patients with KRAS G12 mutations.

Reference:

<https://ir.revmed.com/news-releases/news-release-details/revolution-medicines-announces-fda-breakthrough-therapy>

GFH-375

Cancer type: Pancreatic Cancer

Variant class: KRAS G12D mutation

Supporting Statement:

The FDA has granted Fast Track designation to an oral KRAS G12D (ON/OFF) inhibitor, GFH-375 (VS-7375), for the first-line treatment of patients with KRAS G12D-mutated locally advanced or metastatic adenocarcinoma of the pancreas (PDAC) and for the treatment of patients with KRAS G12D-mutated locally advanced or metastatic PDAC who have received at least one prior line of standard systemic therapy.

Reference:

<https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-granted-fast-track-designation-vs-7375>

Current NCCN Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

NCCN information is current as of 2025-11-03. To view the most recent and complete version of the guideline, go online to [NCCN.org](https://www.nccn.org).

For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

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KRAS p.(G12D) c.35G>A

cetuximab

Cancer type: Colon Cancer

Variant class: KRAS G12 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Patients with any known KRAS mutation (exon 2, 3, 4) or NRAS mutation (exon 2, 3, 4) should not be treated with either cetuximab or panitumumab, unless given as part of a regimen targeting a KRAS G12C mutation."

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]

cetuximab

Cancer type: Rectal Cancer

Variant class: KRAS G12 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Patients with any known KRAS mutation (exons 2, 3, and 4) or NRAS mutation (exons 2, 3, and 4) should not be treated with either cetuximab or panitumumab, unless given as part of a regimen targeting a KRAS G12C mutation."

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]

panitumumab

Cancer type: Colon Cancer

Variant class: KRAS G12 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Patients with any known KRAS mutation (exon 2, 3, 4) or NRAS mutation (exon 2, 3, 4) should not be treated with either cetuximab or panitumumab, unless given as part of a regimen targeting a KRAS G12C mutation."

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]

KRAS p.(G12D) c.35G>A (continued)

panitumumab

Cancer type: Rectal Cancer

Variant class: KRAS G12 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Patients with any known KRAS mutation (exons 2, 3, and 4) or NRAS mutation (exons 2, 3, and 4) should not be treated with either cetuximab or panitumumab, unless given as part of a regimen targeting a KRAS G12C mutation."

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]

Current EMA Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

EMA information is current as of 2025-11-25. For the most up-to-date information, search www.ema.europa.eu.

KRAS p.(G12D) c.35G>A

cetuximab, cetuximab + oxaliplatin

Cancer type: Colorectal Cancer

Label as of: 2025-01-16

Variant class: KRAS G12 mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/erbitux-epar-product-information_en.pdf

panitumumab + oxaliplatin

Cancer type: Colorectal Cancer

Label as of: 2025-05-07

Variant class: KRAS G12 mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/vectibix-epar-product-information_en.pdf

Current ESMO Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

ESMO information is current as of 2025-11-03. For the most up-to-date information, search www.esmo.org.

KRAS p.(G12D) c.35G>A

cetuximab

Cancer type: Colorectal Cancer

Variant class: KRAS G12 mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

- "The presence of RAS mutations is associated with resistance to anti-EGFR mAbs and knowing the expanded RAS mutational status is mandatory for use of both cetuximab and panitumumab, avoiding anti-EGFR mAb treatment when a RAS mutation is confirmed".
- "RAS testing is mandatory before treatment with anti-EGFR mAbs and can be carried out on either the primary tumor or other metastatic sites [III, A]".

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2023); <https://doi.org/10.1016/j.annonc.2022.10.003> (published)]

panitumumab

Cancer type: Colorectal Cancer

Variant class: KRAS G12 mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

- "The presence of RAS mutations is associated with resistance to anti-EGFR mAbs and knowing the expanded RAS mutational status is mandatory for use of both cetuximab and panitumumab, avoiding anti-EGFR mAb treatment when a RAS mutation is confirmed".
- "RAS testing is mandatory before treatment with anti-EGFR mAbs and can be carried out on either the primary tumor or other metastatic sites [III, A]".

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2023); <https://doi.org/10.1016/j.annonc.2022.10.003> (published)]

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, CTNNA1, 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, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYO10, 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 (continued)

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, CBF, 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, ERRF1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, FGF4, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, 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, SLCO1B3, 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, FGFR1, FGFR2, FGFR3, FGR, 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

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBF, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DAX1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRF1, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXW7, FUBP1, GATA3, GNA13, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, ID3, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KEAP1, KLHL13, KMT2A, KMT2B, KMT2C, KMT2D, LARP4B, LATS1, LATS2, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK8, MEN1, MGA, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MTAP, MTUS2, MUTYH, NBN, NCOR1, NF1, NF2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PDCD1, PDCD1LG2, PDIA3, PGD, PHF6, PIK3R1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R2A, PRDM1, PRDM9, PRKAR1A, PSMB10, PSMB8, PSMB9, PTCH1, PTEN, PTPRT, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RASA1, RASA2, RB1, RBM10, RECQL4, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPA1, RPL22, RPL5, RUNX1, RUNX1T1, SDHA, SDHB, SDHC, SDHD, SETD2, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SOCS1, SOX9, SPEN, STAG2, STAT1, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TET2, TGFB2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFH3, ZMYM3, ZRSR2

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ① In this cancer type and other cancer types ✕ No evidence

KRAS p.(G12D) c.35G>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
avutometinib + defactinib	○	○	✕	✕	✕
bevacizumab + CAPOX	✕	✕	✕	○	✕
bevacizumab + FOLFIRI	✕	✕	✕	○	✕
bevacizumab + FOLFOX	✕	✕	✕	○	✕
bevacizumab + FOLFOXIRI	✕	✕	✕	○	✕
ASKC-202, limertinib	✕	✕	✕	✕	● (III)
daraxonrasib	✕	✕	✕	✕	● (III)
daratumumab, TG-01 (Targovax), QS-21 Stimulon, nivolumab	✕	✕	✕	✕	● (II)
afatinib, selumetinib	✕	✕	✕	✕	● (I/II)
almonertinib, palbociclib	✕	✕	✕	✕	● (I/II)
anti-KRAS G12D mTCR	✕	✕	✕	✕	● (I/II)
ARV-806	✕	✕	✕	✕	● (I/II)
DN-022150	✕	✕	✕	✕	● (I/II)
ERAS-0015	✕	✕	✕	✕	● (I/II)
GFH-375	✕	✕	✕	✕	● (I/II)
HRS-4642, SHR-A1904, SHR-1921	✕	✕	✕	✕	● (I/II)
pembrolizumab, chemotherapy, daraxonrasib, RMC-9805	✕	✕	✕	✕	● (I/II)
QLC-1101, QL1203, pembrolizumab (Qilu Pharmaceutical), iparomlimab and tuvonralimab, chemotherapy	✕	✕	✕	✕	● (I/II)
RNK-08954	✕	✕	✕	✕	● (I/II)
TSN-1611	✕	✕	✕	✕	● (I/II)
YL-15293	✕	✕	✕	✕	● (I/II)
zotatifin	✕	✕	✕	✕	● (I/II)
ASP 3082, chemotherapy, pembrolizumab	✕	✕	✕	✕	● (I)
ASP-4396	✕	✕	✕	✕	● (I)
ASP-5834	✕	✕	✕	✕	● (I)
AST-NS2101	✕	✕	✕	✕	● (I)
BDTX-4933	✕	✕	✕	✕	● (I)

* 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

KRAS p.(G12D) c.35G>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BPI-442096	×	×	×	×	● (I)
GDC-7035	×	×	×	×	● (I)
HS-10529	×	×	×	×	● (I)
imatinib, trametinib	×	×	×	×	● (I)
JAB-3312	×	×	×	×	● (I)
KQB-548	×	×	×	×	● (I)
KRAS peptide vaccine, poly-ICLC, nivolumab, ipilimumab	×	×	×	×	● (I)
KRAS TCR, aldesleukin, SLATE 001, chemotherapy	×	×	×	×	● (I)
Nest-1	×	×	×	×	● (I)
NT-112, AZD-0240	×	×	×	×	● (I)
NW-301D	×	×	×	×	● (I)
PT-0253	×	×	×	×	● (I)
QLC-1101	×	×	×	×	● (I)
RMC-9805, daraxonrasib	×	×	×	×	● (I)
toripalimab, chemotherapy, KRAS peptide vaccine	×	×	×	×	● (I)
ZEN-3694, binimetinib	×	×	×	×	● (I)

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

HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	59.58%
BRCA1	LOH, 17q21.31(41197602-41276231)x4
BRCA2	LOH, 13q13.1(32890491-32972932)x3
BRIP1	LOH, 17q23.2(59760627-59938976)x4
CDK12	LOH, 17q12(37618286-37687611)x4
CHEK2	LOH, 22q12.1(29083868-29130729)x4
PALB2	LOH, 16p12.2(23614759-23652528)x4
RAD51C	LOH, 17q22(56769933-56811619)x4
RAD51D	LOH, 17q12(33427950-33446720)x4

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L.

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 (6.2.4 data version 2025.12(007)). 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 and is current as of 2025-11-25. NCCN information was sourced from www.nccn.org and is current as of 2025-11-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-11-25. ESMO information was sourced from www.esmo.org and is current as of 2025-11-03. Clinical Trials information is current as of 2025-11-03. For the most up-to-date information regarding a particular trial, search 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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