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Patient Name: 강규섭
Gender: Male
Sample ID: N26-55

Primary Tumor Site: Lung
Collection Date: 2026.01.21

Sample Cancer Type: Lung Cancer

Report Highlights

2 Relevant Biomarkers
9 Therapies Available
70 Clinical Trials

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.(G12C) c.34G>T***	ROS1	None detected
MET	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	***6.64 Mut/Mb measured***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*KRAS p.(G12C) c.34G>T* KRAS proto-oncogene, GTPase Allele Frequency: 22.75% Locus: chr12:25398285 Transcript: NM_033360.4	**adagrasib** [1, 2 / II+] **sotorasib** [1, 2 / II+]	**adagrasib + cetuximab** [1 / I, II+] **panitumumab + sotorasib** [1 / I, II+] adagrasib [I, II+] adagrasib + panitumumab [I, II+] cetuximab + sotorasib [I, II+] sotorasib [I, II+] bevacizumab + chemotherapy [I]	70
IIC	*IDH1 p.(R132C) c.394C>T* isocitrate dehydrogenase (NADP(+)) 1, cytosolic Allele Frequency: 21.70% Locus: chr2:209113113 Transcript: NM_005896.4	None*	**ivosidenib** [1, 2 / II+] **vorasidenib** [1, 2 / II+]	0

*** Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], 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)

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

KRAS p.(G12C) c.34G>T	**D3S-001** [1], **divarasib** [1], **elironrasib** [1], **olomorasib + pembrolizumab** [1] **avutometinib + sotorasib** [1], **BBO-8520** [1]

Public data sources included in alerts: FDA1, NCCN, **EMA**2, ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources

*MSH6 p.(K1358Dfs*2) c.4068_4071dup, Microsatellite stable, TPMT p.(Y240C) c.719A>G, PTPRT deletion, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
KRAS	p.(G12C)	c.34G>T	COSM516	chr12:25398285	22.75%	NM_033360.4	missense
IDH1	p.(R132C)	c.394C>T	COSM28747	chr2:209113113	21.70%	NM_005896.4	missense
MSH6	p.(K1358Dfs*2)	c.4068_4071dup	.	chr2:48033981	47.73%	NM_000179.3	frameshift Insertion
TPMT	p.(Y240C)	c.719A>G	COSM4986703	chr6:18130918	48.82%	NM_000367.5	missense
MAML3	p.(Q507_Q510del)	c.1455_1479delACAGCAACAGCAACAGCAGCAGCAGinsGCAGCAACAGCAA	.	chr4:140811111	3.13%	NM_018717.5	nonframeshift Block Substitution
MAML3	p.(Q502Tfs*21)	c.1455_1515delACAGCAACAGCAACAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGinsGCAGCAACAGCAACAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGA	.	chr4:140811075	96.88%	NM_018717.5	frameshift Block Substitution
FAT1	p.(T742A)	c.2224A>G	.	chr4:187628758	50.58%	NM_005245.4	missense
MSH3	p.(A61_P63dup)	c.189_190insGCAGCGCCC	.	chr5:79950735	77.94%	NM_002439.5	nonframeshift Insertion
PDE1C	p.(H328N)	c.982C>A	.	chr7:31890304	10.28%	NM_001191058.4	missense
KMT2C	p.(V662L)	c.1984G>T	.	chr7:151945535	18.14%	NM_170606.3	missense
CSMD3	p.(P1922T)	c.5764C>A	.	chr8:113418798	30.27%	NM_198123.2	missense
ARID5B	p.(P461H)	c.1382_1383delCCinsAT	.	chr10:63845643	20.03%	NM_032199.3	missense
MEN1	p.(G310A)	c.929G>C	.	chr11:64573839	46.39%	NM_000244.3	missense
CD276	p.(L325R)	c.974T>G	.	chr15:73996240	49.89%	NM_001024736.2	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
PTPRT	chr20:40710527	0.44	0.65

Biomarker Descriptions

KRAS p.(G12C) c.34G>T

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 HRAS[21]. 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[22,23,24]. Germline mutations in KRAS lead to several genetic disorders known as RASopathies, including Noonan syndrome, which results in heart and congenital defects, growth inhibition, and facial dysmorphic features[25]. Somatic mutations in KRAS are commonly altered in several cancers including non-small cell lung cancer, pancreatic cancer, and multiple myeloma[25].

Alterations and prevalence: The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61[9,26,27]. Mutations at A59, K117, and A146 have also been observed but are less frequent[10,28]. 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[9,10]. 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[9,10]. Alterations in KRAS are also observed in pediatric cancers[10]. 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)[10]. KRAS is amplified in less than 1% of B-lymphoblastic leukemia/lymphoma (1 in 731 cases)[10]. Structural alterations in KRAS are observed in less than 1% of acute lymphoblastic leukemia (1 in 85 cases)[10].

Potential relevance: The FDA has approved the small molecule inhibitors, sotorasib[29] (2021) and adagrasib[30] (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 adenocarcinoma[31]. The FDA has approved the combination of kinase inhibitors, avutometinib and defactinib[32] (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-6036[33], for KRAS G12C-mutated NSCLC. The KRAS-G12C/NRAS-G12C dual inhibitor, elironrasib[34], and the KRAS G12C inhibitor, D3S-001[35], 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, olomorasib[36], was granted breakthrough designation (2025) in combination with pembrolizumab[37] for unresectable advanced or metastatic NSCLC with a KRAS G12C mutation and PD-L1 expression ≥ 50%. The RAF/MEK clamp, avutometinib[38] 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-8520[39], was granted fast track designation in 2025 for previously treated KRAS G12C-mutated patients with metastatic NSCLC. The RAS inhibitor, daraxonrasib[40], was granted breakthrough designation (2025) for previously treated metastatic pancreatic cancer with KRAS G12 mutations. The KRAS G12D (ON/OFF) inhibitor, GFH-375[41], 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-001[42], was granted fast track designation in 2024 for KRAS G12C-mutated patients with advanced unresectable or metastatic colorectal cancers. The PLK1 inhibitor, onvansertib[43], 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, cetuximab[44] and panitumumab[45], 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)[28]. Additionally, KRAS mutations are associated with poor prognosis in NSCLC[46].

IDH1 p.(R132C) c.394C>T

isocitrate dehydrogenase (NADP(+)) 1, cytosolic

Background: The IDH1 and IDH2 genes encode homologous isocitrate dehydrogenase enzymes that catalyze the conversion of isocitrate to α-ketoglutarate (α-KG)[1]. The IDH1 gene encodes the NADP+ dependent cytoplasmic isocitrate dehydrogenase enzyme; IDH2 encodes the mitochondrial isoform[1].

Alterations and prevalence: Recurrent somatic mutations in IDH1 and IDH2 are mutually exclusive and observed in several malignancies, including glioma, chondrosarcoma, intrahepatic cholangiocarcinoma, acute myeloid leukemia (AML), and myelodysplastic syndrome (MDS)[2]. Recurrent IDH1 variants include predominantly R132H/C plus other substitutions at lower frequencies[3]. These gain-of-function variants confer neomorphic enzyme activity[4]. Although wild-type enzymatic activity is ablated,

Biomarker Descriptions (continued)

recurrent IDH1 variants catalyze the conversion of α-KG to D-2-hydroxyglutarate, an oncometabolite with diverse effects on cellular metabolism, epigenetic regulation, redox states, and DNA repair[1,5]. Recurrent IDH1 mutations are present in 5-10% of patients with AML and 5% of patients with MDS[6,7,8]. Recurrent IDH1 mutations are present in nearly 80% of lower-grade diffuse gliomas[9,10]. Alterations in IDH1 are rare in pediatric cancers[9,10]. Somatic mutations in IDH1 are observed in 2% of glioma and less than 1% of leukemia (2 in 311 cases), B-lymphoblastic leukemia/lymphoma (1 in 252 cases), embryonal tumor (1 in 332 cases), and Wilms tumor (1 in 710 cases)[9,10].

Potential relevance: The IDH1 and IDH2 inhibitor vorasidenib[11] is FDA-approved (2024) for the treatment of adults and children with Grade 2 astrocytoma and oligodendroglioma with IDH1 R132C/G/H/L/S mutations. Additionally, olutasidenib[12] (2022) and ivosidenib[13] (2018) are FDA-approved for treating IDH1 R132C/G/H/L/S variants in AML. Ivosidenib is also approved for treating myelodysplastic syndrome (MDS) and cholangiocarcinoma patients with the same IDH1 variants[14]. IDH1 mutations are associated with favorable outcome in lower-grade gliomas, astrocytoma, and oligodendroglioma with 1p/19 codeletion[15,16,17]. Conversely, IDH1 mutations are associated with inferior leukemia-free survival in primary myelofibrosis (PMF)[18,19]. Mutations in IDH1 are diagnostic of IDH-mutated astrocytoma and oligodendroglioma with 1p/19q-codeletion subtypes of central nervous system (CNS) tumors[15,20].

MSH6 p.(K1358Dfs*2) c.4068_4071dup

mutS homolog 6

Background: The MSH6 gene encodes the mutS homolog 6 protein[21]. MSH6 is a tumor suppressor gene that heterodimerizes with MSH2 to form the MutSα complex[47]. The MutSα complex functions in the DNA damage recognition of base-base mismatches or insertion/deletion (indels) of 1-2 nucleotides[47]. DNA damage recognition initiates the mismatch repair (MMR) process that repairs mismatch errors which typically occur during DNA replication[47]. Mutations in MSH2 result in the degradation of MSH6[48]. MSH6, along with MLH1, MSH2, and PMS2, form the core components of the MMR pathway[47]. The MMR pathway is critical to the repair of mismatch errors which typically occur during DNA replication[47]. Deficiency in MMR (dMMR) is characterized by mutations and loss of expression in these genes[49]. dMMR is associated with microsatellite instability (MSI), which is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[50,51,52]. MSI-high (MSI-H) is a hallmark of Lynch Syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in MMR genes[50,53]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[51,53,54,55]. Specifically, MSH6 mutations are associated with an increased risk of ovarian and pancreatic cancer[56,57,58,59].

Alterations and prevalence: Somatic mutations in MSH6 are observed in 11% of uterine corpus endometrial carcinoma, 4% colorectal adenocarcinoma, and 3% skin cutaneous melanoma[9,10]. Alterations in MSH6 are observed in pediatric cancers[9,10]. Somatic mutations are observed in 9% of hepatobiliary cancer, 2% of T-lymphoblastic leukemia/lymphoma, 1% of B-lymphoblastic leukemia/lymphoma, and less than 1% of glioma (2 in 297 cases) and bone cancer (2 in 327 cases)[9,10].

Potential relevance: Pembrolizumab (2014) is an anti-PD-1 immune checkpoint inhibitor that is approved for patients with dMMR solid tumors that have progressed on prior therapies[37]. Nivolumab (2015), an anti-PD-1 immune checkpoint inhibitor, is approved alone or in combination with the cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab (2011), for patients with dMMR colorectal cancer that have progressed on prior treatment[60,61]. MSH6 mutations are consistent with high grade in pediatric diffuse gliomas[62,63].

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 genome[68]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[51,53]. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2[52]. 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 D17S250[69]. 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)[69]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[54,70,71,72,73]. 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 genes[53]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[51,53,54,55].

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[51,53,74,75]. 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[74,75].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[37] (2014) and nivolumab[60] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[37] 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 indication[37]. Dostarlimab[76] (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[71,77]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[61] (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[71,78,79]. 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 patients[79]. 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[80,81]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[80,81].

TPMT p.(Y240C) c.719A>G

thiopurine S-methyltransferase

Background: The TPMT gene encodes thiopurine S-methyltransferase, a cytosolic enzyme that methylates aromatic and heterocyclic sulfhydryl compounds such as thiopurines[21,82,83]. TPMT is the major enzyme responsible for the metabolic inactivation of thiopurine chemotherapeutic drugs used in the treatment of acute lymphoblastic leukemia (ALL), including, 6-mercaptopurine, 6-thioguanine, and azathioprine[82,83,84]. Inherited TPMT polymorphisms, including TPMT*2, TPMT*3A, TPMT*3B, TPMT*3C, and TPMT*8, can result in TPMT deficiency, which is characterized by impaired enzymatic activity and confers an increased risk of severe toxicity to thiopurine drugs due to an increase in systemic drug exposure[82,84].

Alterations and prevalence: Somatic mutations in TPMT are observed in 2% of uterine corpus endometrial carcinoma and colorectal adenocarcinoma[9,10]. Biallelic loss of TPMT is observed in 1% of stomach adenocarcinoma, esophageal adenocarcinoma, and adrenocortical carcinoma[9,10]. Amplification of TPMT is observed in 7% of ovarian serous cystadenocarcinoma, 6% of bladder urothelial carcinoma, 4% of diffuse large B-cell lymphoma, uveal melanoma, uterine carcinosarcoma, and skin cutaneous melanoma, 3% of cholangiocarcinoma, and 2% of breast invasive carcinoma, uterine corpus endometrial carcinoma, and liver hepatocellular carcinoma[9,10]. Alterations in TPMT are also observed in pediatric cancers[10]. Somatic mutations are observed in less than 1% of peripheral nervous system tumors (1 in 1158 cases)[10]. Amplification of TPMT is observed in 1% of peripheral nervous system tumors (1 in 91 cases)[10].

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

PTPRT deletion

protein tyrosine phosphatase, receptor type T

Background: PTPRT encodes protein tyrosine phosphatase receptor type T, part of the protein tyrosine phosphatase (PTP) family which consists of 125 members[21,64,65]. PTPs are responsible for protein dephosphorylation of tyrosine residues and are involved in several cellular processes including proliferation, differentiation, adhesion, and survival[66,67]. Aberrant tyrosine phosphorylation resulting from PTP dysfunction has been linked to cancer progression[66,67].

Alterations and prevalence: Somatic mutations in PTPRT are observed in 29% of skin cutaneous melanoma, 12% of stomach adenocarcinoma and uterine corpus endometrial carcinoma, 10% of colorectal adenocarcinoma and lung adenocarcinoma, 7% of esophageal adenocarcinoma and lung squamous cell carcinoma, 5% of uterine carcinosarcoma and bladder urothelial carcinoma, 4% of head and neck squamous cell carcinoma and cervical squamous cell carcinoma, 3% of glioblastoma multiforme and liver hepatocellular carcinoma, and 2% of diffuse large B-cell lymphoma, pancreatic adenocarcinoma, adrenocortical carcinoma, kidney renal clear cell carcinoma, and ovarian serous cystadenocarcinoma[9,10]. Biallelic loss of PTPRT is observed in about 1% of mesothelioma, prostate adenocarcinoma, and acute myeloid leukemia.[9,10].

Potential relevance: Currently, no therapies are approved for PTPRT 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.(G12C) c.34G>T

panitumumab, panitumumab + sotorasib

Cancer type: Colorectal Cancer **Label as of:** 2025-01-16 **Variant class:** KRAS G12C 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

KRAS p.(G12C) c.34G>T (continued)

cetuximab

Cancer type: Colorectal Cancer **Label as of:** 2021-09-24 **Variant class:** KRAS G12 mutation

Indications and usage:

Erbitux® 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: Erbitux® 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

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D3S-001

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS G12C mutation

Supporting Statement:
The FDA has granted Breakthrough Therapy designation to the KRAS G12C inhibitor, D3S-001, for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) who have had prior treatment with platinum-based chemotherapy and anti-PD-(L)1 antibody but have not been previously treated with a KRAS G12C inhibitor.

Reference:

https://www.prnewswire.com/news-releases/d3-bio-inc-announces-fda-breakthrough-therapy-designation-and-orphan-drug-designation-for-d3s-001-for-the-treatment-of-patients-with-kras-g12c-mutated-cancers-302540808.html

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divarasib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS G12C mutation

Supporting Statement:
The FDA has granted Breakthrough Therapy designation to KRAS G12C inhibitor, GDC-6036, for KRAS G12C mutation in non-small cell lung cancer.

Reference:

https://assets.cwp.roche.com/f/126832/x/5738a7538b/irp230202.pdf

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KRAS p.(G12C) c.34G>T (continued)

elironrasib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS G12C mutation

Supporting Statement:
The FDA has granted Breakthrough designation to KRAS-G12C/NRAS-G12C dual inhibitor, elironrasib, for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer who have received prior chemotherapy and immunotherapy but have not been previously treated with a KRAS G12C inhibitor.

Reference:

https://ir.revmed.com/node/11881/pdf

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olomorasib + pembrolizumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS G12C mutation

Other criteria: PD-L1 overexpression

Supporting Statement:

The FDA has granted Breakthrough Therapy designation to the small molecule inhibitor, olomorasib, in combination with anti-PD-1 therapy pembrolizumab (KEYTRUDA®), for the first-line treatment of patients with unresectable advanced or metastatic non-small cell lung cancer with a KRAS G12C mutation and PD-L1 expression ≥ 50%.

Reference:

https://www.prnewswire.com/news-releases/lillys-olomorasib-receives-us-fdas-breakthrough-therapy-designation-for-the-treatment-of-certain-newly-diagnosed-metastatic-kras-g12c-mutant-lung-cancers-302545643.html

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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

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avutometinib + sotorasib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS G12C mutation

Supporting Statement:
The FDA has granted Fast Track designation to Verastem Oncology's investigational RAF/MEK clamp, avutometinib, in combination with Amgen's KRAS G12C inhibitor, LUMAKRASTM (sotorasib), for the treatment of patients with KRAS G12C-mutant metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy and have not been previously treated with a KRAS G12C inhibitor.

Reference:

https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-granted-fast-track-designation-combination

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KRAS p.(G12C) c.34G>T (continued)

BBO-8520

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS G12C mutation

Supporting Statement:
The FDA has granted Fast Track designation to the KRAS G12C inhibitor, BBO-8520, for the treatment of adult patients with previously treated, $KRAS^{G12C}$-mutated metastatic non-small cell lung cancer (NSCLC).

Reference:

https://www.businesswire.com/news/home/20250109170439/en/

D3S-001

Cancer type: Colorectal Cancer **Variant class:** KRAS G12C mutation

Supporting Statement:

The FDA has granted Fast Track designation to the KRAS G12C inhibitor, D3S-001, for the treatment of KRAS G12C mutated patients with advanced unresectable or metastatic colorectal cancers.

Reference:

https://www.d3bio.com/press-releases/d3-bios-d3s-001-receives-u-s-fda-fast-track-designation-for-the-treatment-of-colorectal-cancer-with-kras-g12c-mutation

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.
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.

KRAS p.(G12C) c.34G>T

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]

KRAS p.(G12C) c.34G>T (continued)

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]

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.(G12C) c.34G>T

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.(G12C) c.34G>T

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, 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, 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, SLCO1B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, 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, 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, ERRFI1, 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, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, 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, CBFB, 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, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRFI1, 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, TGFBR2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFHX3, ZMYM3, ZRSR2

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

KRAS p.(G12C) c.34G>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
adagrasib	●	◑	●	●	● (II)
sotorasib	●	◑	●	●	● (II)
adagrasib + cetuximab	○	○	✖	✖	✖
panitumumab + sotorasib	⚠	○	✖	✖	✖
panitumumab	⚠	✖	✖	✖	✖
adagrasib + panitumumab	✖	○	✖	✖	✖
cetuximab + sotorasib	✖	○	✖	✖	✖
bevacizumab + CAPOX	✖	✖	✖	○	✖
bevacizumab + FOLFIRI	✖	✖	✖	○	✖
bevacizumab + FOLFOX	✖	✖	✖	○	✖
bevacizumab + FOLFOXIRI	✖	✖	✖	○	✖
adagrasib, pembrolizumab, chemotherapy	✖	✖	✖	✖	● (III)
ASKC-202, limertinib	✖	✖	✖	✖	● (III)
D-1553	✖	✖	✖	✖	● (III)
daraxonrasib	✖	✖	✖	✖	● (III)
divarasib, pembrolizumab, chemotherapy	✖	✖	✖	✖	● (III)
glecirasib, JAB-3312, tislelizumab, chemotherapy	✖	✖	✖	✖	● (III)
MK-1084, pembrolizumab	✖	✖	✖	✖	● (III)
olomorasib, durvalumab	✖	✖	✖	✖	● (III)
olomorasib, pembrolizumab, chemotherapy	✖	✖	✖	✖	● (III)
pembrolizumab + berahyaluronidase alfa, chemotherapy, MK-1084	✖	✖	✖	✖	● (III)
sotorasib, pembrolizumab, chemotherapy	✖	✖	✖	✖	● (III)
adagrasib, radiation therapy	✖	✖	✖	✖	● (II)
daratumumab, TG-01 (Targovax), QS-21 Stimulon, nivolumab	✖	✖	✖	✖	● (II)
divarasib	✖	✖	✖	✖	● (II)
glecirasib	✖	✖	✖	✖	● (II)
sintilimab, catequentinib	✖	✖	✖	✖	● (II)
sotorasib, chemotherapy	✖	✖	✖	✖	● (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

KRAS p.(G12C) c.34G>T (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib, selumetinib	✖	✖	✖	✖	● (I/II)
almonertinib, palbociclib	✖	✖	✖	✖	● (I/II)
avutometinib, sotorasib, defactinib	✖	✖	✖	✖	● (I/II)
D-1553, ifebemtinib	✖	✖	✖	✖	● (I/II)
elironrasib, pembrolizumab, chemotherapy, daraxonrasib	✖	✖	✖	✖	● (I/II)
ERAS-0015	✖	✖	✖	✖	● (I/II)
FMC-376	✖	✖	✖	✖	● (I/II)
glecirasib, JAB-3312	✖	✖	✖	✖	● (I/II)
HBI 2376, D-1553	✖	✖	✖	✖	● (I/II)
HS-10370	✖	✖	✖	✖	● (I/II)
HYP-2090PTSA	✖	✖	✖	✖	● (I/II)
YL-15293	✖	✖	✖	✖	● (I/II)
zotatifin, sotorasib	✖	✖	✖	✖	● (I/II)
adagrasib, olaparib	✖	✖	✖	✖	● (I)
ASP-5834	✖	✖	✖	✖	● (I)
BAY-3498264, sotorasib	✖	✖	✖	✖	● (I)
BBO-8520, pembrolizumab	✖	✖	✖	✖	● (I)
BEBT-607	✖	✖	✖	✖	● (I)
BMS-986488, adagrasib	✖	✖	✖	✖	● (I)
BPI-421286	✖	✖	✖	✖	● (I)
BPI-442096	✖	✖	✖	✖	● (I)
carfilzomib, sotorasib	✖	✖	✖	✖	● (I)
darlifarnib, adagrasib	✖	✖	✖	✖	● (I)
elironrasib, daraxonrasib	✖	✖	✖	✖	● (I)
HRS-7058	✖	✖	✖	✖	● (I)
ifebemtinib, sosimerasib, chemotherapy	✖	✖	✖	✖	● (I)
imatinib, trametinib	✖	✖	✖	✖	● (I)
JAB-3312	✖	✖	✖	✖	● (I)
JSKN-016	✖	✖	✖	✖	● (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.(G12C) c.34G>T (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
KQB-365	✖	✖	✖	✖	● (I)
KRAS peptide vaccine, poly-ICLC, nivolumab, ipilimumab	✖	✖	✖	✖	● (I)
ladarixin, sotorasib	✖	✖	✖	✖	● (I)
MK-0472, MK-1084	✖	✖	✖	✖	● (I)
MK-1084	✖	✖	✖	✖	● (I)
Nest-1	✖	✖	✖	✖	● (I)
patritumab deruxtecan	✖	✖	✖	✖	● (I)
sotorasib, radiation therapy	✖	✖	✖	✖	● (I)
SY-5933	✖	✖	✖	✖	● (I)
SYS-6023	✖	✖	✖	✖	● (I)
toripalimab, chemotherapy, KRAS peptide vaccine	✖	✖	✖	✖	● (I)
ZEN-3694, binimetinib	✖	✖	✖	✖	● (I)

IDH1 p.(R132C) c.394C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ivosidenib	○	○	○	○	✖
vorasidenib	○	○	○	✖	✖

* 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	***6.82%***
Not Detected	***Not Applicable***

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 Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine 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.

References

1. Molenaar et al. Wild-type and mutated IDH1/2 enzymes and therapy responses. Oncogene. 2018 Apr;37(15):1949-1960. PMID: 29367755
2. Yan et al. IDH1 and IDH2 mutations in gliomas. N. Engl. J. Med. 2009 Feb 19;360(8):765-73. PMID: 19228619
3. Lu et al. Isocitrate dehydrogenase 1 mutation subtypes at site 132 and their translational potential in glioma. CNS Oncol. 2018 Jan;7(1):41-50. PMID: 29303363
4. Dang et al. Cancer-associated IDH1 mutations produce 2-hydroxyglutarate. Nature. 2009 Dec 10;462(7274):739-44. PMID: 19935646
5. Ward et al. The common feature of leukemia-associated IDH1 and IDH2 mutations is a neomorphic enzyme activity converting alpha-ketoglutarate to 2-hydroxyglutarate. Cancer Cell. 2010 Mar 16;17(3):225-34. PMID: 20171147
6. Paschka et al. IDH1 and IDH2 mutations are frequent genetic alterations in acute myeloid leukemia and confer adverse prognosis in cytogenetically normal acute myeloid leukemia with NPM1 mutation without FLT3 internal tandem duplication. J. Clin. Oncol. 2010 Aug 1;28(22):3636-43. PMID: 20567020
7. Chou et al. The prognostic impact and stability of Isocitrate dehydrogenase 2 mutation in adult patients with acute myeloid leukemia. Leukemia. 2011 Feb;25(2):246-53. PMID: 21079611
8. Marcucci et al. IDH1 and IDH2 gene mutations identify novel molecular subsets within de novo cytogenetically normal acute myeloid leukemia: a Cancer and Leukemia Group B study. J. Clin. Oncol. 2010 May 10;28(14):2348-55. PMID: 20368543
9. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
10. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. Cancer Discov. 2012 May;2(5):401-4. PMID: 22588877
11. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/218784s002lbl.pdf
12. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215814s000lbl.pdf
13. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211192s011lbl.pdf
14. Abou Dalle et al. The role of enasidenib in the treatment of mutant IDH2 acute myeloid leukemia. Ther Adv Hematol. 2018 Jul;9(7):163-173. PMID: 30013764
15. NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2025]
16. Cancer Genome Atlas Research Network. Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. N Engl J Med. 2015 Jun 25;372(26):2481-98. doi: 10.1056/NEJMoa1402121. Epub 2015 Jun 10. PMID: 26061751
17. Houillier et al. IDH1 or IDH2 mutations predict longer survival and response to temozolomide in low-grade gliomas. Neurology. 2010 Oct 26;75(17):1560-6. PMID: 20975057
18. Vannucchi et al. Mutations and prognosis in primary myelofibrosis. Leukemia. 2013 Sep;27(9):1861-9. PMID: 23619563
19. Tefferi et al. IDH1 and IDH2 mutation studies in 1473 patients with chronic-, fibrotic- or blast-phase essential thrombocythemia, polycythemia vera or myelofibrosis. Leukemia. 2010 Jul;24(7):1302-9. PMID: 20508616
20. Louis et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021 Aug 2;23(8):1231-1251. PMID: 34185076
21. O'Leary et al. Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. Nucleic Acids Res. 2016 Jan 4;44(D1):D733-45. PMID: 26553804
22. Pylayeva-Gupta et al. RAS oncogenes: weaving a tumorigenic web. Nat. Rev. Cancer. 2011 Oct 13;11(11):761-74. PMID: 21993244
23. Karnoub et al. Ras oncogenes: split personalities. Nat. Rev. Mol. Cell Biol. 2008 Jul;9(7):517-31. PMID: 18568040
24. Scott et al. Therapeutic Approaches to RAS Mutation. Cancer J. 2016 May-Jun;22(3):165-74. doi: 10.1097/PPO.0000000000000187. PMID: 27341593
25. Johnson et al. Classification of KRAS-Activating Mutations and the Implications for Therapeutic Intervention. Cancer Discov. 2022 Apr 1;12(4):913-923. PMID: 35373279
26. Román et al. KRAS oncogene in non-small cell lung cancer: clinical perspectives on the treatment of an old target. Mol Cancer. 2018 Feb 19;17(1):33. doi: 10.1186/s12943-018-0789-x. PMID: 29455666
27. Dinu et al. Prognostic significance of KRAS gene mutations in colorectal cancer--preliminary study. J Med Life. 2014 Oct-Dec;7(4):581-7. PMID: 25713627
28. Allegra et al. Extended RAS Gene Mutation Testing in Metastatic Colorectal Carcinoma to Predict Response to Anti-Epidermal Growth Factor Receptor Monoclonal Antibody Therapy: American Society of Clinical Oncology Provisional Clinical Opinion Update 2015. J. Clin. Oncol. 2016 Jan 10;34(2):179-85. PMID: 26438111
29. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/214665Orig1s009correctedlbl.pdf
30. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/216340s005lbl.pdf

References (continued)

31. NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 2.2025]
32. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219616s000lbl.pdf
33. https://assets.cwp.roche.com/f/126832/x/5738a7538b/irp230202.pdf
34. https://ir.revmed.com/node/11881/pdf
35. https://www.prnewswire.com/news-releases/d3-bio-inc-announces-fda-breakthrough-therapy-designation-and-orphan-drug-designation-for-d3s-001-for-the-treatment-of-patients-with-kras-g12c-mutated-cancers-302540808.html
36. https://www.prnewswire.com/news-releases/lillys-olomorasib-receives-us-fdas-breakthrough-therapy-designation-for-the-treatment-of-certain-newly-diagnosed-metastatic-kras-g12c-mutant-lung-cancers-302545643.html
37. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125514s178lbl.pdf
38. https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-granted-fast-track-designation-combination
39. https://www.businesswire.com/news/home/20250109170439/en/
40. https://ir.revmed.com/news-releases/news-release-details/revolution-medicines-announces-fda-breakthrough-therapy
41. https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-granted-fast-track-designation-vs-7375
42. https://www.d3bio.com/press-releases/d3-bios-d3s-001-receives-u-s-fda-fast-track-designation-for-the-treatment-of-colorectal-cancer-with-kras-g12c-mutation
43. https://cardiffoncology.com/wp-content/uploads/2021/07/Cardiff_Oncology_Investor_Presentation-_July_2021.pdf
44. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125084s279lbl.pdf
45. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125147s213lbl.pdf
46. Slebos et al. K-ras oncogene activation as a prognostic marker in adenocarcinoma of the lung. N. Engl. J. Med. 1990 Aug 30;323(9):561-5. PMID: 2199829
47. Li. Mechanisms and functions of DNA mismatch repair. Cell Res. 2008 Jan;18(1):85-98. PMID: 18157157
48. Zhao et al. Mismatch Repair Deficiency/Microsatellite Instability-High as a Predictor for anti-PD-1/PD-L1 Immunotherapy Efficacy. J Hematol Oncol. 12(1),54. PMID: 31151482
49. Martin et al. Therapeutic targeting of the DNA mismatch repair pathway. Clin Cancer Res. 2010 Nov 1;16(21):5107-13. PMID: 20823149
50. Lynch et al. Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. Clin. Genet. 2009 Jul;76(1):1-18. PMID: 19659756
51. Baudrin et al. Molecular and Computational Methods for the Detection of Microsatellite Instability in Cancer. Front Oncol. 2018 Dec 12;8:621. doi: 10.3389/fonc.2018.00621. eCollection 2018. PMID: 30631754
52. Saeed et al. Microsatellites in Pursuit of Microbial Genome Evolution. Front Microbiol. 2016 Jan 5;6:1462. doi: 10.3389/fmicb.2015.01462. eCollection 2015. PMID: 26779133
53. Nojadeh et al. Microsatellite instability in colorectal cancer. EXCLI J. 2018;17:159-168. PMID: 29743854
54. Imai et al. Carcinogenesis and microsatellite instability: the interrelationship between genetics and epigenetics. Carcinogenesis. 2008 Apr;29(4):673-80. PMID: 17942460
55. Latham et al. Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. J. Clin. Oncol. 2019 Feb 1;37(4):286-295. PMID: 30376427
56. Bonadona et al. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. JAMA. 2011 Jun 8;305(22):2304-10. PMID: 21642682
57. Engel et al. Risks of less common cancers in proven mutation carriers with lynch syndrome. J Clin Oncol. 2012 Dec 10;30(35):4409-15. PMID: 23091106
58. Grant et al. Prevalence of germline mutations in cancer predisposition genes in patients with pancreatic cancer. Gastroenterology. 2015 Mar;148(3):556-64. PMID: 25479140
59. Hu et al. Association Between Inherited Germline Mutations in Cancer Predisposition Genes and Risk of Pancreatic Cancer. JAMA. 2018 Jun 19;319(23):2401-2409. PMID: 29922827
60. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125554s131lbl.pdf
61. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125377s136lbl.pdf
62. Buccoliero et al. Pediatric High Grade Glioma Classification Criteria and Molecular Features of a Case Series. Genes (Basel). 2022 Mar 31;13(4). PMID: 35456430

References (continued)

63. Friker et al. MSH2, MSH6, MLH1, and PMS2 immunohistochemistry as highly sensitive screening method for DNA mismatch repair deficiency syndromes in pediatric high-grade glioma. Acta Neuropathol. 2025 Feb 2;149(1):11. PMID: 39894875
64. Xie et al. Regulatory Functions of Protein Tyrosine Phosphatase Receptor Type O in Immune Cells. Front Immunol. 2021;12:783370. PMID: 34880876
65. Alonso et al. The extended human PTPome: a growing tyrosine phosphatase family. FEBS J. 2016 Jun;283(11):2197-201. PMID: 27263510
66. Kumar et al. Activity-based probes for protein tyrosine phosphatases. Proc Natl Acad Sci U S A. 2004 May 25;101(21):7943-8. PMID: 15148367
67. Tonks. Protein tyrosine phosphatases: from genes, to function, to disease. Nat Rev Mol Cell Biol. 2006 Nov;7(11):833-46. PMID: 17057753
68. Lander et al. Initial sequencing and analysis of the human genome. Nature. 2001 Feb 15;409(6822):860-921. PMID: 11237011
69. Boland et al. A National Cancer Institute Workshop on Microsatellite Instability for cancer detection and familial predisposition: development of international criteria for the determination of microsatellite instability in colorectal cancer. Cancer Res. 1998 Nov 15;58(22):5248-57. PMID: 9823339
70. Halford et al. Low-level microsatellite instability occurs in most colorectal cancers and is a nonrandomly distributed quantitative trait. Cancer Res. 2002 Jan 1;62(1):53-7. PMID: 11782358
71. NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]
72. Pawlik et al. Colorectal carcinogenesis: MSI-H versus MSI-L. Dis. Markers. 2004;20(4-5):199-206. PMID: 15528785
73. Lee et al. Low-Level Microsatellite Instability as a Potential Prognostic Factor in Sporadic Colorectal Cancer. Medicine (Baltimore). 2015 Dec;94(50):e2260. PMID: 26683947
74. Cortes-Ciriano et al. A molecular portrait of microsatellite instability across multiple cancers. Nat Commun. 2017 Jun 6;8:15180. doi: 10.1038/ncomms15180. PMID: 28585546
75. Bonneville et al. Landscape of Microsatellite Instability Across 39 Cancer Types. JCO Precis Oncol. 2017;2017. PMID: 29850653
76. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761174s009lbl.pdf
77. NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]
78. Ribic et al. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. N. Engl. J. Med. 2003 Jul 17;349(3):247-57. PMID: 12867608
79. Klingbiel et al. Prognosis of stage II and III colon cancer treated with adjuvant 5-fluorouracil or FOLFIRI in relation to microsatellite status: results of the PETACC-3 trial. Ann. Oncol. 2015 Jan;26(1):126-32. PMID: 25361982
80. Hermel et al. The Emerging Role of Checkpoint Inhibition in Microsatellite Stable Colorectal Cancer. J Pers Med. 2019 Jan 16;9(1). PMID: 30654522
81. Ciardiello et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy. Cancer Treat. Rev. 2019 Jun;76:22-32. PMID: 31079031
82. Katara et al. TPMT Polymorphism: When Shield Becomes Weakness. Interdiscip Sci. 2016 Jun;8(2):150-155. PMID: 26297310
83. Yong et al. The role of pharmacogenetics in cancer therapeutics. Br J Clin Pharmacol. 2006 Jul;62(1):35-46. PMID: 16842377
84. McLeod et al. Genetic polymorphism of thiopurine methyltransferase and its clinical relevance for childhood acute lymphoblastic leukemia. Leukemia. 2000 Apr;14(4):567-72. PMID: 10764140