

**Patient Name:** 이영호  
**Gender:** M  
**Sample ID:** N26-56

**Primary Tumor Site:** lung  
**Collection Date:** 2026.01.15

## 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	<b>KRAS p.(Q61H) c.183A&gt;C</b>	ROS1	None detected
MET	None detected		

  

Genomic Alteration	Finding
Tumor Mutational Burden	<b>2.85 Mut/Mb measured</b>

## Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	<b>PIK3CA p.(H1047R) c.3140A&gt;G</b> phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha Allele Frequency: 5.70% Locus: chr3:178952085 Transcript: NM_006218.4	None*	<b>inavolisib + palbociclib + hormone therapy</b> <sup>1, 2 / I</sup> <b>alpelisib + hormone therapy</b> <sup>1, 2 / II+</sup> <b>capivasertib + hormone therapy</b> <sup>1, 2 / II</sup> + aspirin <sup>II+</sup>	6
IIC	<b>KRAS p.(Q61H) c.183A&gt;C</b> KRAS proto-oncogene, GTPase Allele Frequency: 4.72% Locus: chr12:25380275 Transcript: NM_033360.4	None*	<b>avotemetinib + defactinib</b> <sup>1 / II+</sup> bevacizumab + chemotherapy <sup>I</sup>	5

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

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

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

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

## Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, TPMT p.(Y240C) c.719A>G, 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
PIK3CA	p.(H1047R)	c.3140A>G	COSM775	chr3:178952085	5.70%	NM_006218.4	missense
KRAS	p.(Q61H)	c.183A>C	COSM554	chr12:25380275	4.72%	NM_033360.4	missense
TPMT	p.(Y240C)	c.719A>G	COSM4986703	chr6:18130918	50.90%	NM_000367.5	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	48.30%	NM_000903.3	missense
POLR1A	p.(I225V)	c.673A>G	.	chr2:86315746	3.16%	NM_015425.6	missense
BMPR2	p.(F446L)	c.1338T>G	.	chr2:203407095	54.24%	NM_001204.7	missense
HLA-A	p.(I121R)	c.362_363delTAinsGG	.	chr6:29911063	43.24%	NM_001242758.1	missense
KMT2C	p.(P860S)	c.2578C>T	.	chr7:151935866	27.30%	NM_170606.3	missense
AMER1	p.(A229P)	c.685G>C	.	chrX:63412482	100.00%	NM_152424.4	missense

## Biomarker Descriptions

### PIK3CA p.(H1047R) c.3140A>G

*phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha*

**Background:** The PIK3CA gene encodes the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha of the class I phosphatidylinositol 3-kinase (PI3K) enzyme<sup>53</sup>. PI3K is a heterodimer that contains a p85 regulatory subunit, which couples one of four p110 catalytic subunits to activated tyrosine protein kinases<sup>54,55</sup>. The p110 catalytic subunits include p110α, β, δ, γ and are encoded by genes PIK3CA, PIK3CB, PIK3CD, and PIK3CG, respectively<sup>54</sup>. PI3K catalyzes the conversion of phosphatidylinositol (4,5)-bisphosphate (PI(4,5)P2) into phosphatidylinositol (3,4,5)-trisphosphate (PI(3,4,5)P3) while the phosphatase and tensin homolog (PTEN) catalyzes the reverse reaction<sup>56,57</sup>. The reversible phosphorylation of inositol lipids regulates diverse aspects of cell growth and metabolism<sup>56,57,58,59</sup>. Recurrent somatic alterations in PIK3CA are frequent in cancer and result in the activation of PI3K/AKT/MTOR pathway, which can influence several hallmarks of cancer including cell proliferation, apoptosis, cancer cell metabolism and invasion, and genetic instability<sup>60,61,62</sup>.

**Alterations and prevalence:** Activating mutations in PIK3CA commonly occur in exons 10 and 21 (previously referred to as exons 9 and 20 due to exon 1 being untranslated)<sup>63,64</sup>. These mutations typically cluster in the exon 10 helical (codons E542/E545) and exon 21 kinase (codon H1047) domains, each having distinct mechanisms of activation<sup>65,66,67</sup>. Somatic mutations in PIK3CA are observed in 50% of uterine corpus endometrial carcinoma, 35% of uterine carcinosarcoma, 32% of breast invasive carcinoma, 29% of cervical squamous cell carcinoma, 28% of colorectal adenocarcinoma, 22% of bladder urothelial carcinoma, 17% of head and neck squamous cell carcinoma, 16% of stomach adenocarcinoma, 11% of lung squamous cell carcinoma, 9% of esophageal adenocarcinoma, 8% of brain lower grade glioma, 6% of cholangiocarcinoma, 5% of skin cutaneous melanoma and lung adenocarcinoma, 4% of liver hepatocellular carcinoma, 3% of pancreatic adenocarcinoma and sarcoma, and 2% of mesothelioma, prostate adenocarcinoma, testicular germ cell tumors, and ovarian serous cystadenocarcinoma<sup>6,9</sup>. PIK3CA is amplified in 38% of lung squamous cell carcinoma, 20% of ovarian serous cystadenocarcinoma, 18% of esophageal adenocarcinoma, 16% of head and neck squamous cell carcinoma, 15% of cervical squamous cell carcinoma, 11% of uterine carcinosarcoma, 7% of uterine corpus endometrial carcinoma, 5% of stomach adenocarcinoma, 4% of bladder urothelial carcinoma, 3% of breast invasive carcinoma and pancreatic adenocarcinoma, and 2% of prostate adenocarcinoma, lung adenocarcinoma, and kidney renal clear cell carcinoma<sup>6,9</sup>. Alterations in PIK3CA are also observed in pediatric cancers<sup>9</sup>. Somatic mutations in PIK3CA are observed in 6% of non-Hodgkin Lymphoma (1 in 17 cases), 4% of glioma (11 in 297 cases), 3% of soft tissue sarcoma (1 in 38 patients), 2% of embryonal tumors (6 in 332 cases), 1% of leukemia (5 in 354 cases), and less than 1% of bone cancer (3 in 327 cases), B-lymphoblastic leukemia/lymphoma (2 in 252 cases), and peripheral nervous system tumors (1 in 1158 cases)<sup>9</sup>.

## Biomarker Descriptions (continued)

**Potential relevance:** The PI3K inhibitor, alpelisib<sup>68</sup>, is FDA-approved (2019) in combination with fulvestrant for the treatment of patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced or metastatic breast cancer. Specifically, exon 21 H1047R mutations were associated with more durable clinical responses in comparison to exon 10 E545K mutations<sup>69</sup>. However, alpelisib did not improve response when administered with letrozole in patients with ER + early breast cancer with PIK3CA mutations<sup>70</sup>. The FDA also approved the kinase inhibitor, capivasertib (2023)<sup>71</sup> in combination with fulvestrant for locally advanced or metastatic HR-positive, HER2-negative breast cancer with one or more PIK3CA/AKT1/PTEN-alterations following progression after endocrine treatment. The kinase inhibitor, inavolisib<sup>72</sup>, is also FDA-approved (2024) in combination with palbociclib and fulvestrant for the treatment of adults with endocrine-resistant, PIK3CA-mutated, HR-positive, and HER2-negative breast cancer. Case studies with mTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers<sup>73,74</sup>. In colorectal cancers, PIK3CA mutations predict significantly improved survival and reduced disease recurrence with adjuvant aspirin therapy, compared to no benefit in wild-type PIK3CA tumors<sup>36,44,75,76</sup>. In 2025, the FDA granted fast track designation to the PI3K $\alpha$  inhibitor and degrader, ETX-636<sup>77</sup>, for the treatment of PIK3CA-mutant, HR-positive/HER-negative advanced breast cancer.

### KRAS p.(Q61H) c.183A>C

*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<sup>1</sup>. 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<sup>2,3,4</sup>. 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<sup>5</sup>. Somatic mutations in KRAS are commonly altered in several cancers including non-small cell lung cancer, pancreatic cancer, and multiple myeloma<sup>5</sup>.

**Alterations and prevalence:** The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61<sup>6,7,8</sup>. Mutations at A59, K117, and A146 have also been observed but are less frequent<sup>9,10</sup>. 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<sup>6,9</sup>. 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<sup>6,9</sup>. Alterations in KRAS are also observed in pediatric cancers<sup>9</sup>. 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)<sup>9</sup>. KRAS is amplified in less than 1% of B-lymphoblastic leukemia/lymphoma (1 in 731 cases)<sup>9</sup>. Structural alterations in KRAS are observed in less than 1% of acute lymphoblastic leukemia (1 in 85 cases)<sup>9</sup>.

**Potential relevance:** The FDA has approved the small molecule inhibitors, sotorasib<sup>11</sup> (2021) and adagrasib<sup>12</sup> (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<sup>13</sup>. The FDA has approved the combination of kinase inhibitors, avutometinib and defactinib<sup>14</sup> (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<sup>15</sup>, for KRAS G12C-mutated NSCLC. The KRAS-G12C/NRAS-G12C dual inhibitor, elironrasib<sup>16</sup>, and the KRAS G12C inhibitor, D3S-001<sup>17</sup>, 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<sup>18</sup>, was granted breakthrough designation (2025) in combination with pembrolizumab<sup>19</sup> for unresectable advanced or metastatic NSCLC with a KRAS G12C mutation and PD-L1 expression  $\geq$  50%. The RAF/MEK clamp, avutometinib<sup>20</sup> 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<sup>21</sup>, was granted fast track designation in 2025 for previously treated KRAS G12C-mutated patients with metastatic NSCLC. The RAS inhibitor, daraxonrasib<sup>22</sup>, was granted breakthrough designation (2025) for previously treated metastatic pancreatic cancer with KRAS G12 mutations. The KRAS G12D (ON/OFF) inhibitor, GFH-375<sup>23</sup>, 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<sup>24</sup>, was granted fast track designation in 2024 for KRAS G12C-mutated patients with advanced unresectable or metastatic colorectal cancers. The PLK1 inhibitor, onvansertib<sup>25</sup>, 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<sup>26</sup> and panitumumab<sup>27</sup>, are contraindicated for treatment of colorectal

## Biomarker Descriptions (continued)

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)<sup>10</sup>. Additionally, KRAS mutations are associated with poor prognosis in NSCLC<sup>28</sup>.

### 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<sup>29</sup>. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue<sup>30,31</sup>. 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<sup>32</sup>. 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<sup>33</sup>. 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)<sup>33</sup>. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS<sup>34,35,36,37,38</sup>. 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<sup>31</sup>. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer<sup>30,31,35,39</sup>.

**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<sup>30,31,40,41</sup>. 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<sup>40,41</sup>.

**Potential relevance:** Anti-PD-1 immune checkpoint inhibitors including pembrolizumab<sup>19</sup> (2014) and nivolumab<sup>42</sup> (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab<sup>19</sup> is also approved 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<sup>19</sup>. Dostarlimab<sup>43</sup> (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<sup>36,44</sup>. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab<sup>45</sup> (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<sup>36,46,47</sup>. 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<sup>47</sup>. 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<sup>48,49</sup>. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers<sup>48,49</sup>.

### 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<sup>1,50,51</sup>. 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<sup>50,51,52</sup>. 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<sup>50,52</sup>.

**Alterations and prevalence:** Somatic mutations in TPMT are observed in 2% of uterine corpus endometrial carcinoma and colorectal adenocarcinoma<sup>6,9</sup>. Biallelic loss of TPMT is observed in 1% of stomach adenocarcinoma, esophageal adenocarcinoma, and adrenocortical carcinoma<sup>6,9</sup>. 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<sup>6,9</sup>. Alterations in TPMT are also observed in pediatric cancers<sup>9</sup>. Somatic mutations are observed in less than 1% of peripheral nervous system tumors (1 in 1158 cases)<sup>9</sup>. Amplification of TPMT is observed in 1% of peripheral nervous system tumors (1 in 91 cases)<sup>9</sup>.

**Potential relevance:** Currently, no therapies are approved for TPMT 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](http://www.fda.gov).

### KRAS p.(Q61H) c.183A>C

#### cetuximab

**Cancer type:** Colorectal Cancer

**Label as of:** 2021-09-24

**Variant class:** KRAS Q61 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](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125084s279lbl.pdf)

## KRAS p.(Q61H) c.183A>C (continued)

### panitumumab

**Cancer type:** Colorectal Cancer

**Label as of:** 2025-01-16

**Variant class:** KRAS Q61 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](https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125147s213lbl.pdf)

## 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](http://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.(Q61H) c.183A>C

### cetuximab

**Cancer type:** Colon Cancer

**Variant class:** KRAS Q61 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.(Q61H) c.183A>C (continued)

### cetuximab

Cancer type: Rectal Cancer

Variant class: KRAS Q61 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 Q61 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 Q61 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](http://www.ema.europa.eu).

## KRAS p.(Q61H) c.183A>C

### cetuximab, cetuximab + oxaliplatin

Cancer type: Colorectal Cancer

Label as of: 2025-01-16

Variant class: KRAS Q61 mutation

**Reference:**

[https://www.ema.europa.eu/en/documents/product-information/erbitux-epar-product-information\\_en.pdf](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 Q61 mutation

**Reference:**

[https://www.ema.europa.eu/en/documents/product-information/vectibix-epar-product-information\\_en.pdf](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](http://www.esmo.org).

### KRAS p.(Q61H) c.183A>C

#### cetuximab

Cancer type: Colorectal Cancer

Variant class: KRAS Q61 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 Q61 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, PXDN, 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, PXDN, 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, DSC1, 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   
  In this cancer type and other cancer types   
  No evidence

### PIK3CA p.(H1047R) c.3140A>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alpelisib + fulvestrant	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
capiwasertib + fulvestrant	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
inavolisib + palbociclib + fulvestrant	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
aspirin	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
ETX-636	<input checked="" type="radio"/> (I/II)				
HTL-0039732, atezolizumab	<input checked="" type="radio"/> (I/II)				
STX-478, hormone therapy	<input checked="" type="radio"/> (I/II)				
JS-105	<input checked="" type="radio"/> (I)				
RLY-2608	<input checked="" type="radio"/> (I)				
SNV-4818, hormone therapy	<input checked="" type="radio"/> (I)				

### KRAS p.(Q61H) c.183A>C

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
avutometinib + defactinib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
bevacizumab + CAPOX	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
bevacizumab + FOLFIRI	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
bevacizumab + FOLFOX	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
bevacizumab + FOLFOXIRI	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
daraxonrasib	<input checked="" type="radio"/> (III)				
ERAS-0015	<input checked="" type="radio"/> (I/II)				
zotatifin	<input checked="" type="radio"/> (I/II)				
Nest-1	<input checked="" type="radio"/> (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	<b>0.0%</b>
Not Detected	<b>Not Applicable</b>

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.

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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](http://www.fda.gov) and is current as of 2025-11-25. NCCN information was sourced from [www.nccn.org](http://www.nccn.org) and is current as of 2025-11-03. EMA information was sourced from [www.ema.europa.eu](http://www.ema.europa.eu) and is current as of 2025-11-25. ESMO information was sourced from [www.esmo.org](http://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](http://www.clinicaltrials.gov) by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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