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**Patient Name:** 오웅록
**Gender:** M
**Sample ID:** N25-51
**Primary Tumor Site:** Colon
**Collection Date:** 2025.05.28

## Sample Cancer Type: Colon Cancer

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### Report Highlights
1 Relevant Biomarkers
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## Relevant Colon Cancer Findings

| Gene | Finding | Gene | Finding |
|---|---|---|---|
| BRAF | None detected | NTRK2 | None detected |
| ERBB2 | None detected | NTRK3 | None detected |
| KRAS | ***KRAS p.(G12D) c.35G>A*** | POLD1 | None detected |
| NRAS | None detected | POLE | None detected |
| NTRK1 | None detected | RET | None detected |

| Genomic Alteration | Finding |
|---|---|
| Tumor Mutational Burden | ***5.67 Mut/Mb measured*** |

HRD Status: ***HR Proficient (HRD-)***

## Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|
| IA | *KRAS p.(G12D) c.35G>A*<br>KRAS proto-oncogene, GTPase<br>Allele Frequency: 27.77%<br>Locus: chr12:25398284<br>Transcript: NM_033360.4 | bevacizumab + chemotherapy [I] | None* | 29 |

*** 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.

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

| | |
|---|---|
| *KRAS p.(G12D) c.35G>A* | ⊘ **cetuximab** [1, 2], **cetuximab + chemotherapy** [2], **panitumumab** [1], **panitumumab + chemotherapy** [2] |

**Public data sources included in alerts: FDA**[1], NCCN, **EMA**[2], ESMO

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

*APC p.(E918*) c.2752G>T, APC p.(K1437Tfs*16) c.4310_4314delAAACA, HLA-A p.(L180*) c.539T>A, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden*

# Variant Details

## DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Variant ID | Locus | Allele Frequency | Transcript | Variant Effect |
|---|---|---|---|---|---|---|---|
| KRAS | p.(G12D) | c.35G>A | COSM521 | chr12:25398284 | 27.77% | NM_033360.4 | missense |
| APC | p.(E918*) | c.2752G>T | . | chr5:112174043 | 15.75% | NM_000038.6 | nonsense |
| APC | p.(K1437Tfs*16) | c.4310_4314delAAACA | . | chr5:112175599 | 19.84% | NM_000038.6 | frameshift Deletion |
| HLA-A | p.(L180*) | c.539T>A | . | chr6:29911240 | 69.43% | NM_001242758.1 | nonsense |
| NQO1 | p.(P187S) | c.559C>T | . | chr16:69745145 | 52.75% | NM_000903.3 | missense |
| PGD | p.(R297K) | c.890G>A | . | chr1:10477089 | 6.91% | NM_002631.4 | missense |
| ATR | p.(E226Q) | c.676G>C | . | chr3:142281568 | 3.61% | NM_001184.4 | missense |
| MAML3 | p.(Q491Pfs*32) | c.1472_1506delAGCAGCAGCAGCAGCAGCAGCAGCAGCAGinsCAGCAGCAGCAGCAGCAGCAA | . | chr4:140811084 | 46.67% | NM_018717.5 | frameshift Block Substitution |
| MAML3 | p.(Q488_Q494delinsHDS) | c.1464_1506delGCAACAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGinsCGACAGCCAGCAGCAGCAGCAGCAGCAA | . | chr4:140811084 | 53.33% | NM_018717.5 | nonframeshift Block Substitution |
| GLI3 | p.(P941T) | c.2821C>A | . | chr7:42005850 | 73.14% | NM_000168.6 | missense |
| DCDC1 | p.(P44L) | c.131C>T | . | chr11:31349697 | 69.99% | NM_001367979.1 | missense |
| SMG6 | p.(G333D) | c.998G>A | . | chr17:2203049 | 19.21% | NM_017575.5 | missense |
| PTPRT | p.(R260W) | c.778C>T | . | chr20:41385183 | 56.25% | NM_133170.4 | missense |

## Copy Number Variations

| Gene | Locus | Copy Number | CNV Ratio |
|---|---|---|---|
| ATM | chr11:108098341 | 2 | 0.96 |
| CHEK1 | chr11:125496639 | 2 | 1.01 |

## Biomarker Descriptions

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

*KRAS proto-oncogene, GTPase*

Background: The KRAS proto-oncogene encodes a GTPase that functions in signal transduction and is a member of the RAS superfamily which also includes NRAS and HRAS. 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[1,2,3].

Alterations and prevalence: Recurrent mutations in RAS oncogenes cause constitutive activation and are found in 20-30% of cancers. KRAS mutations are observed in up to 10-20% of uterine cancer, 30-35% of lung adenocarcinoma and colorectal cancer, and about 60% of pancreatic cancer[4]. The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61[4,5,6]. Mutations at A59, K117, and A146 have also been observed but are less frequent[7,8].

Potential relevance: The FDA has approved the small molecule inhibitors, sotorasib[9] (2021) and adagrasib[10] (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[11]. The FDA has also granted breakthrough therapy designation (2022) to the KRAS G12C inhibitor, GDC-6036[12], for KRAS G12C-mutated non-small cell lung cancer. The SHP2 inhibitor, BBP-398[13] was granted fast track designation (2022) in combination with sotorasib for previously treated patients with KRAS G12C-mutated metastatic NSCLC. The RAF/MEK clamp, avutometinib[14] was also granted fast track designation (2024) in combination with sotorasib for KRAS G12C-mutated metastatic NSCLC 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[15], was granted fast track designation in 2025 for previously treated KRAS G12C-mutated patients with metastatic NSCLC. The KRAS G12C inhibitor, D3S-001[16], was granted fast track designation in 2024 for KRAS G12C-mutated patients with advanced unresectable or metastatic colorectal cancers. The PLK1 inhibitor, onvansertib[17], 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[18] and panitumumab[19], 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)[8]. Additionally, KRAS mutations are associated with poor prognosis in NSCLC[20].

**APC p.(E918*) c.2752G>T, APC p.(K1437Tfs*16) c.4310_4314delAAACA**

*APC, WNT signaling pathway regulator*

Background: The APC gene encodes the adenomatous polyposis coli tumor suppressor protein that plays a crucial role in regulating the β-catenin/WNT signaling pathway which is involved in cell migration, adhesion, proliferation, and differentiation[28]. APC is an antagonist of WNT signaling as it targets β-catenin for proteasomal degradation[29,30]. Germline mutations in APC are predominantly inactivating and result in an autosomal dominant predisposition for familial adenomatous polyposis (FAP) which is characterized by numerous polyps in the intestine[28,31]. Acquiring a somatic mutation in APC is considered to be an early and possibly initiating event in colorectal cancer[32].

Alterations and prevalence: Somatic mutations in APC are observed in up to 65% of colorectal cancer, and in up to 15% of stomach adenocarcinoma and uterine corpus endometrial carcinoma[4,7,33]. In colorectal cancer, ~60% of somatic APC mutations have been reported to occur in a mutation cluster region (MCR) resulting in C-terminal protein truncation and APC inactivation[34,35].

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

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

*major histocompatibility complex, class I, A*

Background: The HLA-A gene encodes the major histocompatibility complex, class I, A[21]. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells[22]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[23]. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self[24,25,26]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-A[27].

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

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

# Alerts Informed By Public Data Sources

## Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2025-04-16. For the most up-to-date information, search www.fda.gov.

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

### cetuximab

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

**Indications and usage:**

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

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

### panitumumab

**Cancer type:** Colorectal Cancer **Label as of:** 2025-01-16 **Variant class:** KRAS G12 mutation

**Indications and usage:**

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

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

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

KRAS G12C-mutated Metastatic Colorectal Cancer (mCRC)*

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

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

**Reference:**

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

## Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2025-04-01. 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.(G12D) c.35G>A

### cetuximab

**Cancer type:** Colon Cancer **Variant class:** KRAS G12 mutation

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

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

**Reference:** NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2025]

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

### 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 2.2025]

### cetuximab

**Cancer type:** Rectal Cancer **Variant class:** KRAS G12 mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "Patients with any known KRAS mutation (exons 2, 3, and 4) or NRAS mutation (exons 2, 3, and 4) should not be treated with either cetuximab or panitumumab, unless given as part of a regimen targeting a KRAS G12C mutation."

**Reference:** NCCN Guidelines® - NCCN-Rectal Cancer [Version 2.2025]

### 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 2.2025]

## Current EMA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

EMA information is current as of 2025-04-16. For the most up-to-date information, search www.ema.europa.eu.

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

### cetuximab, cetuximab + oxaliplatin

**Cancer type:** Colorectal Cancer **Label as of:** 2025-01-16 **Variant class:** KRAS G12 mutation

**Reference:**

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

### panitumumab + oxaliplatin

**Cancer type:** Colorectal Cancer **Label as of:** 2022-07-06 **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 2025-04-01. For the most up-to-date information, search www.esmo.org.

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

#### cetuximab

**Cancer type:** Colorectal Cancer **Variant class:** KRAS G12 mutation

**Summary:**
ESMO Clinical Practice Guidelines include the following supporting statement:

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

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

#### panitumumab

**Cancer type:** Colorectal Cancer **Variant class:** KRAS G12 mutation

**Summary:**
ESMO Clinical Practice Guidelines include the following supporting statement:

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

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

## Genes Assayed

### Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, 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.(G12D) c.35G>A

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| bevacizumab + CAPOX | ✖ | ✖ | ✖ | ● | ✖ |
| bevacizumab + FOLFIRI | ✖ | ✖ | ✖ | ● | ✖ |
| bevacizumab + FOLFOX | ✖ | ✖ | ✖ | ● | ✖ |
| bevacizumab + FOLFOXIRI | ✖ | ✖ | ✖ | ● | ✖ |
| bevacizumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| fruquintinib, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| regorafenib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| tunlametinib, vemurafenib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| afatinib, selumetinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| anti-KRAS G12D mTCR | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| DN-022150 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| GDC-7035 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| GFH-375 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| HRS-4642, adebrelimab, SHR-9839, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| IMM-1-104 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| TSN-1611 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| YL-15293 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| ASP-4396 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| AST-NS2101 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| HMPL-415 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| IX-001 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| JAB-3312 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| KRAS peptide vaccine, poly-ICLC, nivolumab, ipilimumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| KRAS TCR, aldesleukin, SLATE 001, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (I) |
| KRAS-EphA-2-CAR-DC, anti-PD-1, ipilimumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| Nest-1 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| NW-301D | ✖ | ✖ | ✖ | ✖ | ● (I) |
| PT-0253 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| QLC-1101 | ✖ | ✖ | ✖ | ✖ | ● (I) |

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

## Relevant Therapy Summary (continued)

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

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

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| RMC-6236 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| RMC-9805, RMC-6236 | ✖ | ✖ | ✖ | ✖ | ● (I) |

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

Thermo Fisher Scientific's Ion Torrent 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 (6.1.1 data version 2025.05(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 2025-04-16. NCCN information was sourced from www.nccn.org and is current as of 2025-04-01. EMA information was sourced from www.ema.europa.eu and is current as of 2025-04-16. ESMO information was sourced from www.esmo.org and is current as of 2025-04-01. Clinical Trials information is current as of 2025-04-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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