



Sample Information

Patient Name: 柯明輝
Gender: Male
ID No.: A123846265
History No.: 49771304
Age: 67

Ordering Doctor: DOC3064F 陳育民
Ordering REQ.: D787K2M
Signing in Date: 2023/10/04

Path No.: M112-00261
MP No.: F23073
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S112-46783B
Percentage of tumor cells: 30%

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Table of Contents	Page	Report Highlights
Variant Details	2	1 Relevant Biomarkers
Biomarker Descriptions	2	3 Therapies Available
Relevant Therapy Summary	3	8 Clinical Trials
Relevant Therapy Details	4	
Clinical Trials Summary	11	
Alert Details	12	

Relevant Non-Small Cell Lung Cancer Variants

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		

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: 37.44%	adagrasib ¹ sotorasib ^{1, 2}	adagrasib bevacizumab + chemotherapy sotorasib	8

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

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.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
KRAS	p.(G12C)	c.34G>T	COSM516	chr12:25398285	37.44%	NM_033360.4	missense	1998
KIT	p.(M541L)	c.1621A>C	.	chr4:55593464	51.93%	NM_000222.3	missense	1997
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.45%	NM_213647.3	missense	2000
FGFR4	p.(T179A)	c.535A>G	.	chr5:176518037	55.83%	NM_213647.3	missense	1999

Biomarker Descriptions

KRAS (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 cancer⁴. 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, sotorasib⁹ (2021) and adagrasib¹⁰ (2022), for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC). The FDA has also granted breakthrough therapy designation (2022) to the KRAS G12C inhibitor, GDC-6036¹¹, for KRAS G12C mutation in non-small cell lung cancer. The small molecular inhibitor, RO-5126766, was granted breakthrough designation (2021) alone for KRAS G12V mutant non-small cell lung cancer or in combination with defactinib, for KRAS mutant endometrial carcinoma and KRAS G12V mutant non-small cell lung cancer¹². The PLK1 inhibitor, onvansertib¹³, 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). Additionally, the SHP2 inhibitor, BBP-398¹⁴ was granted fast track designation (2022) in combination with sotorasib for previously treated patients with KRAS G12C-mutated metastatic NSCLC. The EGFR antagonists, cetuximab¹⁵ and panitumumab¹⁶, 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 NSCLC¹⁷.

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*
sotorasib	●	◐	●	●	✕
adagrasib	●	◐	✕	●	✕
bevacizumab + CAPOX	✕	✕	✕	○	✕
bevacizumab + FOLFIRI	✕	✕	✕	○	✕
bevacizumab + FOLFOX	✕	✕	✕	○	✕
bevacizumab + FOLFOXIRI	✕	✕	✕	○	✕
JDQ-443	✕	✕	✕	✕	● (III)
adagrasib, pembrolizumab, chemotherapy	✕	✕	✕	✕	● (II/III)
GDC-6036	✕	✕	✕	✕	● (II/III)
D-1553	✕	✕	✕	✕	● (I/II)
GDC-6036, pembrolizumab	✕	✕	✕	✕	● (I/II)
JDQ-443, TNO-155, tislelizumab	✕	✕	✕	✕	● (I/II)
sotorasib, afatinib, pembrolizumab, atezolizumab, chemotherapy, BI-1701963	✕	✕	✕	✕	● (I/II)
RMC-6291	✕	✕	✕	✕	● (I)

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

Relevant Therapy Details

Current FDA Information

☒ In this cancer type ☐ In other cancer type ☐ In this cancer type and other cancer types

FDA information is current as of 2023-08-16. For the most up-to-date information, search www.fda.gov.

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

● adagrasib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-12-12

Variant class: KRAS G12C mutation

Indications and usage:

KRAZATI™ is an inhibitor of the RAS GTPase family indicated for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA approved test, who have received at least one prior systemic therapy.

This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial(s).

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216340Orig1s000Corrected_lbl.pdf

● sotorasib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-24

Variant class: KRAS G12C mutation

Indications and usage:

LUMAKRAS® is an inhibitor of the RAS GTPase family indicated for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy. This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214665s004lbl.pdf

Current NCCN Information

- ☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

NCCN information is current as of 2023-08-01. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

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

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

☒ adagrasib

Cancer type: Non-Small Cell Lung Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

☒ adagrasib

Cancer type: Non-Small Cell Lung Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression (Subsequent therapy, Second-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

☒ sotorasib

Cancer type: Non-Small Cell Lung Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression (Subsequent therapy, Second-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

☐ adagrasib

Cancer type: Pancreatic Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic, Locally Advanced, Recurrent (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 2.2023]

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

☐ sotorasib

Cancer type: Pancreatic Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic, Locally Advanced, Recurrent (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 2.2023]

☐ adagrasib

Cancer type: Pancreatic Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic, Locally Advanced, Recurrent (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 2.2023]

☐ sotorasib

Cancer type: Pancreatic Cancer

Variant class: KRAS G12C mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic, Locally Advanced, Recurrent (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 2.2023]

Current EMA Information

☒ In this cancer type ☐ In other cancer type ☐ In this cancer type and other cancer types

EMA information is current as of 2023-08-16. For the most up-to-date information, search www.ema.europa.eu/ema.

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

☒ sotorasib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-11-29

Variant class: KRAS G12C mutation

Reference:

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

Current ESMO Information

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

ESMO information is current as of 2023-08-01. For the most up-to-date information, search www.esmo.org.

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

☒ sotorasib

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

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):

- Stage IV; Metastatic, Advanced (Subsequent therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

☒ adagrasib

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

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

☐ bevacizumab + CAPOX

Cancer type: Colorectal Cancer Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):

- Stage IV; Unresectable (First-line therapy); ESMO-MCBS v1.1 score: 1

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

☐ bevacizumab + FOLFOX

Cancer type: Colorectal Cancer Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):

- Stage IV; Unresectable (First-line therapy); ESMO-MCBS v1.1 score: 1

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

KRAS p.(G12C) c.34G>T (continued)**○ bevacizumab + FOLFOXIRI**

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):

- Stage IV; Unresectable (First-line therapy); ESMO-MCBS v1.1 score: 2

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

○ bevacizumab + CAPOX

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: II / A

Population segment (Line of therapy):

- Resectable (Line of therapy not specified)

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

○ bevacizumab + FOLFIRI

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: II / A

Population segment (Line of therapy):

- Resectable (Line of therapy not specified)

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

○ bevacizumab + FOLFOX

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: II / A

Population segment (Line of therapy):

- Resectable (Line of therapy not specified)

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

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

○ bevacizumab + FOLFOXIRI

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

ESMO Level of Evidence/Grade of Recommendation: II / A

Population segment (Line of therapy):

- Resectable (Line of therapy not specified)

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

Clinical Trials in Taiwan region:



Clinical Trials Summary

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

NCT ID	Title	Phase
NCT05132075	A Randomized, Controlled, Open Label, Phase III Study Evaluating the Efficacy and Safety of JDQ443 Versus Docetaxel in Previously Treated Subjects With Locally Advanced or Metastatic KRAS G12C Mutant Non-small Cell Lung Cancer	III
NCT04613596	A Phase II Trial of MRTX849 Monotherapy and in Combination With Pembrolizumab and a Phase III Trial of Adagrasib in Combination With Pembrolizumab Versus Pembrolizumab Plus Chemotherapy in Patients With Advanced Non-Small Cell Lung Cancer With KRAS G12C Mutation	II/III
NCT03178552	A Phase II/III Multicenter Study Evaluating the Efficacy and Safety of Multiple Targeted Therapies as Treatments for Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) Harboring Actionable Somatic Mutations Detected in Blood (B-FAST: Blood-First Assay Screening Trial)	II/III
NCT05789082	A PHASE IB/II, OPEN-LABEL, MULTICENTER STUDY EVALUATING THE SAFETY, ACTIVITY, AND PHARMACOKINETICS OF GDC-6036 IN COMBINATION WITH OTHER ANTI-CANCER THERAPIES IN PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED OR METASTATIC NON SMALL CELL LUNG CANCER WITH A KRAS G12C MUTATION	I/II
NCT04699188	A Phase Ib/II Open-label, Multi-center Dose Escalation Study of JDQ443 in Patients With Advanced Solid Tumors Harboring the KRAS G12C Mutation	I/II
NCT04185883	A Phase Ib/II, Protocol Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Sotorasib Monotherapy and in Combination With Other Anti-cancer Therapies in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	I/II
NCT04585035	A Phase I/II, Open Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of D-1553 in Subjects With Advanced or Metastatic Solid Tumors With KRasG12C Mutation	I/II
NCT05462717	Phase I/Ib, Multicenter, Open-Label, Dose Escalation and Dose Expansion Study of RMC-6291 Monotherapy in Subjects With Advanced KRASG12C Mutant Solid Tumors	I

Alerts Informed By Public Data Sources

Current FDA Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

FDA information is current as of 2023-08-16. For the most up-to-date information, search www.fda.gov.

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

cetuximab

Cancer type: Colorectal Cancer

Label as of: 2021-09-24

Variant class: KRAS G12 mutation

Indications and usage:

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

Head and Neck Cancer

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

Colorectal Cancer

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

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

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

BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)

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

Reference:

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

panitumumab

Cancer type: Colorectal Cancer

Label as of: 2021-08-25

Variant class: KRAS G12 mutation

Indications and usage:

VECTIBIX® is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use) 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.
- **Limitation of Use:** VECTIBIX® is not indicated for the treatment of patients with RAS-mutant mCRC or for whom RAS mutation status is unknown.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125147s210lbl.pdf

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

GDC-6036

Cancer type: Non-Small Cell Lung Cancer

Variant class: KRAS G12C mutation

Supporting Statement:

The FDA has granted breakthrough 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>

BBP-398 + sotorasib

Cancer type: Non-Small Cell Lung Cancer,
Solid Tumor

Variant class: KRAS G12C mutation

Supporting Statement:

The FDA has granted Fast Track Designation to a SHP2 inhibitor, BBP-398, in combination with LUMAKRAS for adult patients with previously treated KRAS G12C-mutated metastatic NSCLC.

Reference:

<https://bridgebio.com/news/bridgebio-pharma-announces-first-lung-cancer-patient-dosed-in-phase-1-2-trial-and-us-fda-fast-track-designation-for-shp2-inhibitor-bbp-398-in-combination-with-amgens-lumakras-sotorasib/>

bevacizumab + onvansertib + FOLFIRI

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Supporting Statement:

The FDA has granted Fast Track Designation to the Polo-like Kinase 1 (PLK1) inhibitor, onvansertib, in combination with FOLFIRI and bevacizumab, for KRAS mutations in metastatic colorectal cancer in the second line.

Reference:

<https://cardiffoncology.investorroom.com/2020-05-28-Cardiff-Oncology-Announces-Fast-Track-Designation-Granted-by-the-FDA-to-Onvansertib-for-Second-Line-Treatment-of-KRAS-Mutated-Colorectal-Cancer>

Current NCCN Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

NCCN information is current as of 2023-08-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

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

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

cetuximab

Cancer type: Colon Cancer

Variant class: KRAS exon 2 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."

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2023]

cetuximab

Cancer type: Rectal Cancer

Variant class: KRAS exon 2 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."

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2023]

panitumumab

Cancer type: Colon Cancer

Variant class: KRAS exon 2 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."

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2023]

panitumumab

Cancer type: Rectal Cancer

Variant class: KRAS exon 2 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."

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2023]

Current EMA Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

EMA information is current as of 2023-08-16. For the most up-to-date information, search www.ema.europa.eu/ema.

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

cetuximab, cetuximab + oxaliplatin

Cancer type: Colorectal Cancer

Label as of: 2022-05-25

Variant class: KRAS exon 2 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 exon 2 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 2023-08-01. 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 exon 2 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)]

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

panitumumab

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 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)]

References

1. Pylayeva-Gupta et al. RAS oncogenes: weaving a tumorigenic web. *Nat. Rev. Cancer*. 2011 Oct 13;11(11):761-74. PMID: 21993244
2. Karnoub et al. Ras oncogenes: split personalities. *Nat. Rev. Mol. Cell Biol.* 2008 Jul;9(7):517-31. PMID: 18568040
3. Scott et al. Therapeutic Approaches to RAS Mutation. *Cancer J.* 2016 May-Jun;22(3):165-74. doi: 10.1097/PPO.000000000000187. PMID: 27341593
4. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat. Genet.* 2013 Oct;45(10):1113-20. PMID: 24071849
5. 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
6. 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
7. 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
8. 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
9. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214665s004lbl.pdf
10. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216340Orig1s000Corrected_lbl.pdf
11. <https://assets.cwp.roche.com/f/126832/x/5738a7538b/irp230202.pdf>
12. <https://investor.verastem.com//news-releases/news-release-details/verastem-oncology-reports-third-quarter-2022-financial-results>
13. <https://cardiffoncology.investorroom.com/2020-05-28-Cardiff-Oncology-Announces-Fast-Track-Designation-Granted-by-the-FDA-to-Onvansertib-for-Second-Line-Treatment-of-KRAS-Mutated-Colorectal-Cancer>
14. <https://bridgebio.com/news/bridgebio-pharma-announces-first-lung-cancer-patient-dosed-in-phase-1-2-trial-and-us-fda-fast-track-designation-for-shp2-inhibitor-bbp-398-in-combination-with-amgens-lumakras-sotorasib/>
15. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125084s279lbl.pdf
16. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125147s210lbl.pdf
17. 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