



Sample Information

Patient Name: 陳中吉**Gender:** Male**ID No.:** E100254843**History No.:** 45951506**Age:** 64**Ordering Doctor:** DOC6386G 吳智中**Ordering REQ.:** 0AYDQQE**Signing in Date:** 2020/11/12**Path No.:** S109-89833**MP No.:** F20096**Assay:** Oncomine Focus Assay**Sample Type:** FFPE**Block No.:** S109-75485G**Percentage of tumor cells:** 80%**Note:**

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	Not detected	NTRK3	Not detected
ERBB2	Not detected	RET	Not detected
KRAS	KRAS p.(G12C) c.34G>T	ROS1	Not detected
MET	Not detected		



Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	KRAS p.(G12C) c.34G>T KRAS proto-oncogene, GTPase Allele Fraction: 0.401	None	cabozantinib	52

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 Fraction	Transcript	Variant Effect	Coverage
KRAS	p.(G12C)	c.34G>T	COSM516	chr12:25398285	0.401	NM_033360.3	missense	1995
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	0.485	NM_004304.4	missense	1997
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	0.995	NM_004304.4	missense	1998
ALK	p.(=)	c.3375C>A	.	chr2:29445458	0.513	NM_004304.4	synonymous	1996
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	0.997	NM_000142.4	synonymous	1998
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	0.999	NM_006206.5	synonymous	1997
KIT	p.(=)	c.1266G>T	.	chr4:55589784	0.061	NM_000222.2	synonymous	1998
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	0.988	NM_213647.2	missense	2000
RET	p.(=)	c.2307G>T	.	chr10:43613843	0.528	NM_020975.4	synonymous	1995
ERBB2	p.(=)	c.2379G>A	.	chr17:37881050	0.532	NM_004448.3	synonymous	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: Currently, no therapies are approved for KRAS aberrations. However, the KRAS G12C inhibitor, sotorasib (AMG 510)⁹, was granted fast track designation (2019) for previously treated non-small cell lung cancer (NSCLC) patients with KRAS G12C mutations. Additionally, onvansertib¹⁰ was granted fast track designation (2020) for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). The EGFR antagonists, cetuximab¹¹ and panitumumab¹², are contraindicated for



Biomarker Descriptions (continued)

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 NSCLC¹³.

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*
cabozantinib	✕	✕	✕	○	✕
bevacizumab, chemotherapy	✕	✕	✕	✕	● (III)
lenvatinib, pembrolizumab, chemotherapy	✕	✕	✕	✕	● (III)
sotorasib	✕	✕	✕	✕	● (III)
atezolizumab, cobimetinib	✕	✕	✕	✕	● (II)
ceralasertib + durvalumab	✕	✕	✕	✕	● (II)
regorafenib, chemotherapy	✕	✕	✕	✕	● (II)
selumetinib, ulixertinib	✕	✕	✕	✕	● (II)
sintilimab, anlotinib hydrochloride	✕	✕	✕	✕	● (II)
spartalizumab	✕	✕	✕	✕	● (II)
targeted therapy, chemotherapy	✕	✕	✕	✕	● (II)
TVB-2640	✕	✕	✕	✕	● (II)
afatinib, selumetinib	✕	✕	✕	✕	● (I/II)
ASTX029	✕	✕	✕	✕	● (I/II)
avelumab, binimetinib, talazoparib	✕	✕	✕	✕	● (I/II)
binimetinib + palbociclib, binimetinib, palbociclib	✕	✕	✕	✕	● (I/II)
HH-2710	✕	✕	✕	✕	● (I/II)
lapatinib, trametinib	✕	✕	✕	✕	● (I/II)
mirdametinib, lifirafenib	✕	✕	✕	✕	● (I/II)
MRTX849, pembrolizumab, cetuximab, afatinib	✕	✕	✕	✕	● (I/II)
navitoclax, trametinib	✕	✕	✕	✕	● (I/II)

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



Relevant Therapy Summary (continued)

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ✕ No evidence

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
neratinib, valproic acid	✕	✕	✕	✕	● (I/II)
rigosertib, nivolumab	✕	✕	✕	✕	● (I/II)
RMC-4630, cobimetinib	✕	✕	✕	✕	● (I/II)
RO-5126766, defactinib	✕	✕	✕	✕	● (I/II)
selinexor, chemotherapy	✕	✕	✕	✕	● (I/II)
selumetinib, durvalumab, tremelimumab	✕	✕	✕	✕	● (I/II)
sotorasib, pembrolizumab	✕	✕	✕	✕	● (I/II)
TNO-155, MRTX849	✕	✕	✕	✕	● (I/II)
zotatifin	✕	✕	✕	✕	● (I/II)
BGB-3245	✕	✕	✕	✕	● (I)
BI-1701963, trametinib	✕	✕	✕	✕	● (I)
cobimetinib, belvarafenib	✕	✕	✕	✕	● (I)
FCN-437	✕	✕	✕	✕	● (I)
GDC-6036	✕	✕	✕	✕	● (I)
JAB-3312	✕	✕	✕	✕	● (I)
JSI-1187	✕	✕	✕	✕	● (I)
LXH254, LTT-462, trametinib, ribociclib	✕	✕	✕	✕	● (I)
LXH254, spartalizumab	✕	✕	✕	✕	● (I)
LY3214996, midazolam, abemaciclib, chemotherapy, encorafenib, cetuximab	✕	✕	✕	✕	● (I)
MLN-2480	✕	✕	✕	✕	● (I)
mRNA-5671, pembrolizumab	✕	✕	✕	✕	● (I)
NBF-006	✕	✕	✕	✕	● (I)
neratinib, trametinib	✕	✕	✕	✕	● (I)
pembrolizumab + trametinib	✕	✕	✕	✕	● (I)
RMC-4630	✕	✕	✕	✕	● (I)

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



Relevant Therapy Summary (continued)

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
RMC-4630, pembrolizumab	×	×	×	×	● (I)
RO-5126766	×	×	×	×	● (I)
RO-5126766, everolimus	×	×	×	×	● (I)
sotorasib, PD-1 Inhibitor, Pan-ErbB tyrosine kinase inhibitor	×	×	×	×	● (I)
TAK 659, chemotherapy	×	×	×	×	● (I)
TNO-155, spartalizumab	×	×	×	×	● (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 ESMO Information

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

ESMO information is current as of 2020-09-01. For the most up-to-date information, search www.esmo.org.

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

☐ cabozantinib

Cancer type: Thyroid Gland Medullary Carcinoma Variant class: RAS mutation

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

Population segment (Line of therapy):

- Metastatic Thyroid Gland Medullary Carcinoma (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Thyroid Cancer [Annals of Oncology 30: 1856–1883, 2019 doi:10.1093/annonc/mdz400]



Clinical Trials Summary

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

NCT ID	Title	Phase
NCT04303780	A Phase III Multicenter, Randomized, Open Label, Active-controlled, Study of AMG 510 Versus Docetaxel for the Treatment of Previously Treated Locally Advanced and Unresectable or Metastatic NSCLC Subjects With Mutated KRAS p.G12C	III
NCT02743923	Chemotherapy in KRAS Mutated Chemotherapy Naive Non-small Cell Lung Cancer Patients: a Phase III Study Comparing Cisplatin-pemetrexed With Carboplatin-paclitaxel-bevacizumab: NVALT 22	III
NCT03829319	A Phase III Randomized, Placebo-controlled Study to Evaluate the Safety and Efficacy of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) With or Without Lenvatinib (E7080/MK-7902) as First-line Intervention in Participants With Metastatic Nonsquamous Non-small Cell Lung Cancer (LEAP-006)	III
NCT03600701	A Phase II Study of Atezolizumab and Cobimetinib in PD-1/PD-L1 Inhibitor Resistant or Refractory Non-Small Cell Lung Cancer	II
NCT02664935	National Lung Matrix Trial: Multi-drug, Genetic Marker-directed, Non-comparative, Multi-centre, Multi-arm Phase II Trial in Non-small Cell Lung Cancer	II
NCT03520842	Study of Regorafenib in Combination With Oral Methotrexate for KRAS Mutated Non-Small Cell Lung Cancer (NSCLC)	II
No NCT ID	Safety and Efficacy of Sintilimab Combined With Anlotinib in Patients With KRAS Mutant Advanced / Metastatic Non-Small Cell Lung Cancer: a Prospective, Single-Arm Study	II
NCT03693326	An Open-Label, Multicenter, Phase II Study of PDR001 in Patients with Non-Small Cell Lung Cancer Harboring KRAS/NRAS Mutation or Without Actionable Genetic Abnormalities, Detected Using NGS Platform	II
No NCT ID	A Single-center, Open-label, Non-randomized Control Clinical Trial On Clinical Features and Medical Treatment of Advanced NSCLC With Rare Gene Mutations	II
NCT03808558	A Phase II Single-Center Pharmacodynamic Study of TVB-2640 In KRAS Mutant Non-Small Cell Lung Carcinomas	II
NCT03785249	A Phase I/II Multiple Expansion Cohort Trial of MRTX849 in Patients With Advanced Solid Tumors With KRAS G12C Mutation KRYSTAL-1	I/II
NCT03600883	A Phase I/II, Open-label Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of AMG 510 Monotherapy in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation and AMG 510 Combination Therapy in Subjects With Advanced NSCLC With KRAS p.G12C	I/II
NCT04330664	A Phase I/II Trial of MRTX849 in Combination With TNO155 in Patients With Advanced Solid Tumors With KRAS G12C Mutation	I/II
NCT03095612	An Investigator-Sponsored, Phase I/II Trial of the Oral XPO1 Inhibitor Selinexor (KPT-330) in Combination With Docetaxel for Previously Treated, Advanced KRAS Mutant Non-small Cell Lung Cancer (NSCLC)	I/II
NCT02450656	Phase I/II Study With the Combination of Afatinib and Selumetinib in Advanced KRAS Mutant Positive and PIK3CA Wildtype Non-small Cell Lung Cancer	I/II
NCT02230553	Phase I/II Study With Lapatinib Plus Trametinib in Patients With Metastatic KRAS Mutant Non-small Cell Lung Cancer	I/II



Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
NCT03637491	A Phase Ib/II Study To Evaluate Safety And Clinical Activity Of Combinations Of Avelumab, Binimetinib And Talazoparib In Patients With Locally Advanced Or Metastatic Ras-Mutant Solid Tumors	I/II
NCT03170206	Phase I/II Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the MEK Inhibitor Binimetinib (MEK162) for Patients With Advanced KRAS Mutant Non-Small Cell Lung Cancer	I/II
NCT03905148	A Phase Ib, Open-Label, Dose-escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activities of a RAF Dimer Inhibitor BGB-283 in Combination With MEK Inhibitor PD-0325901 in Patients With Advanced or Refractory Solid Tumors	I/II
NCT04263090	A Phase I/IIa Study of Rigosertib Plus Nivolumab in Stage IV Lung Adenocarcinoma Patients With KRAS Mutation Who Progressed on First-Line Treatment	I/II
NCT03875820	FRAME: A Phase I Trial Of The Combination Of VS-6063 (FAK Inhibitor) And RO5126766 (CH5126766) (A Dual RAF/MEK Inhibitor) In Patients With Advanced Solid Tumours.	I/II
NCT03581487	Phase I/II Trial Immunotherapy With Durvalumab and Tremelimumab With Continuous or Intermittent MEK Inhibitor Selumetinib in NSCLC	I/II
NCT03948763	A Phase I, Open-Label, Multicenter Study to Assess the Safety and Tolerability of mRNA-5671/V941 as a Monotherapy and in Combination With Pembrolizumab in Participants With KRAS Mutant Advanced or Metastatic Non-Small Cell Lung Cancer, Colorectal Cancer or Pancreatic Adenocarcinoma	I
NCT03634982	A Phase I, Open-Label, Multicenter, Dose-Escalation Study of RMC-4630 Monotherapy in Adult Participants with Relapsed/Refractory Solid Tumors	I
NCT04185883	A Phase Ib, Protocol Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of AMG 510 (p1NN) Sotorasib Monotherapy and in Combination With Other Anti-cancer Therapies in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	I
NCT04000529	A Phase Ib, Open-label, Multi-center Study to Characterize the Safety, Tolerability, and Preliminary Efficacy of TNO155 in Combination With Spaltalizumab or Ribociclib in Selected Malignancies	I
NCT04045496	A Phase I, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Evidence of Antitumor Activity of JAB-3312 in Adult Patients With Advanced Solid Tumors	I
NCT04111458	A Phase I Open-label Dose Escalation Trial of BI 1701963 as Monotherapy and in Combination With Trametinib in Patients With KRAS Mutated Advanced or Metastatic Solid Tumours	I
NCT03951116	Phase I Study of FCN-437c in Patients with Advanced Solid Tumors	I
NCT02974725	A Phase Ib, Open-label, Multicenter Study of Oral LXH254-centric Combinations in Adult Patients With Advanced or Metastatic KRAS or BRAF Mutant Non-Small Cell Lung Cancer or NRAS Mutant Melanoma	I
NCT02607813	A Phase I Dose Finding Study of Oral LXH254 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations	I
NCT03819387	A Phase I/Ib Open-Label, Multi-Center, Dose-Escalation Study to Investigate the Safety, Pharmacokinetics and Preliminary Efficacy of Intravenous NBF 006 in Patients With Non-Small Cell Lung, Pancreatic, or Colorectal Cancer	I
NCT03299088	A Phase Ib Trial of Pembrolizumab (MK-3475) and Trametinib Focused on Advanced KRAS Mutant Non-small Cell Lung Cancer	I



Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
NCT04418661	A Phase I, Open-label, Multicenter, Safety Study of SAR442720 in Combination With Pembrolizumab in Patients With Advanced Malignancies	I
NCT03681483	A Phase I Trial of RO5126766 (CH5126766) in Patients With Advanced KRAS-Mutant Lung Adenocarcinomas	I
NCT02857270	A Phase I Study of an ERK1/2 Inhibitor (LY3214996) Administered Alone or in Combination With Other Agents in Advanced Cancer	I
NCT03155620	NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol	II
NCT02079740	An Open Label, Two-Part, Phase Ib/II Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of the MEK Inhibitor Trametinib and the BCL2-Family Inhibitor Navitoclax (ABT-263) in Combination in Subjects With KRAS or NRAS Mutation-Positive Advanced Solid Tumors	I/II
NCT04092673	A Phase I-II Dose-Escalation and Cohort-Expansion Study of Intravenous eFT226 in Subjects With Selected Advanced Solid Tumor Malignancies	I/II
NCT03919292	Phase 1/2 Study of Neratinib and Divalproex Sodium (Valproate) in Advanced Solid Tumors, With an Expansion Cohort in Ras-Mutated Cancers	I/II
NCT03989115	A Phase Ib/II, Open-Label, Multicenter Dose-Escalation and Dose-Expansion Study of the Combination of RMC-4630 and Cobimetinib in Adult Participants With Relapsed/Refractory Solid Tumors With Specific Genomic Aberrations	I/II
NCT04198818	A First-in-Human, Open Label, Phase I/II Study to Evaluate the Safety, Tolerability and Pharmacokinetics of HH2710 in Patients With Advanced Tumors	I/II
NCT03520075	A Phase I/II Study of the Safety, Pharmacokinetics, and Activity of ASTX029 in Subjects With Advanced Solid Tumors	I/II
NCT04449874	A Phase I Dose-Escalation and Dose-Expansion Study Evaluating the Safety, Pharmacokinetics, and Activity of GDC-6036 in Patients With Advanced or Metastatic Solid Tumors With a KRAS G12C Mutation	I
NCT04380753	A Phase I, Open-label Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of AMG 510 (p1NN Sotorasib) in Subjects of Chinese Descent With Advanced/Metastatic Solid Tumors With KRAS p.G12C Mutation (CodeBreak 105)	I
NCT04249843	A First-in-Human, Phase Ia/Ib, Open Label, Dose-Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics, and Antitumor Activity of the RAF Dimer Inhibitor BGB-3245 in Patients With Advanced or Refractory Tumors	I
NCT04418167	A Phase I Study of ERK1/2 Inhibitor JSI-1187 Administered as Monotherapy and in Combination With Dabrafenib for the Treatment of Advanced Solid Tumors With MAPK Pathway Mutations	I
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/Amplification, or HER3/4 Mutation or KRAS Mutation	I
NCT02407509	A Phase I Trial of RO5126766 (a Dual RAF/MEK Inhibitor) Exploring Intermittent, Oral Dosing Regimens in Patients With Solid Tumours or Multiple Myeloma, With an Expansion to Explore Intermittent Dosing in Combination With Everolimus	I



Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
NCT03756818	A Phase I Study of TAK-659 and Paclitaxel in Patients With Advanced Solid Tumors	I
NCT03284502	A Phase Ib, Open-label, Multicenter, Dose Escalation Study of the Safety, Tolerability, and Pharmacokinetics of Cobimetinib and HM95573 in Patients With Locally Advanced or Metastatic Solid Tumors	I
NCT03429803	A Phase I Study of TAK-580 (MLN2480) for Children With Low-Grade Gliomas and Other RAS/RAF/MEK/ERK Pathway Activated Tumors	I

Alerts Informed By Public Data Sources

Current FDA Information

⊘ Contraindicated
 ⊖ Not recommended
 ⚠ Resistance

FDA information is current as of 2020-09-16. 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: 2019-04-23

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.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125084s273lbl.pdf



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

⊘ panitumumab

Cancer type: Colorectal Cancer

Label as of: 2017-06-29

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/2017/125147s207lbl.pdf

Current NCCN Information

⊘ Contraindicated ⊖ Not recommended ⊔ Resistance

NCCN information is current as of 2020-09-01. For the most up-to-date information, search www.nccn.org.
 For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

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 4.2020]

⊘ 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 6.2020]



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

⊘ 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 4.2020]

⊘ 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 6.2020]

Current EMA Information

⊘ Contraindicated ⊖ Not recommended 🛡 Resistance

EMA information is current as of 2020-09-16. 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: 2020-01-30

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: 2020-01-24

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

ESMO information is current as of 2020-09-01. 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:

- "It has been demonstrated that the (potential) benefit of anti-EGFR antibodies in all treatment lines and either as a single agent or in combination with any chemotherapy regimen is limited to patients in whom a RAS mutation is excluded. It was shown that the 'expanded RAS' analysis (also including the detection of mutations in exons 3 and 4 of the KRAS gene as well as mutations in the NRAS [exons 2-4] gene) is superior to the KRAS (exon 2) analysis in predicting both more efficacy in the expanded RAS wild-type (WT) patients and a potential detrimental effect in patients harbouring any RAS mutation in their tumour genome [II/A]."

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9. (eUpdate: 20 September 2016; Corrigendum: 21 July 2015)]

⊘ cetuximab + chemotherapy

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

- "It has been demonstrated that the (potential) benefit of anti-EGFR antibodies in all treatment lines and either as a single agent or in combination with any chemotherapy regimen is limited to patients in whom a RAS mutation is excluded. It was shown that the 'expanded RAS' analysis (also including the detection of mutations in exons 3 and 4 of the KRAS gene as well as mutations in the NRAS [exons 2-4] gene) is superior to the KRAS (exon 2) analysis in predicting both more efficacy in the expanded RAS wild-type (WT) patients and a potential detrimental effect in patients harbouring any RAS mutation in their tumour genome [II/A]."
- "Thus, the activity of the anti-EGFR antibodies is confined to RAS WT tumours (and not only KRAS WT tumours). This is true for the combinations of cetuximab or panitumumab alone or with irinotecan- and oxaliplatin-based regimens. Treatment with anti-EGFR antibodies may even harm patients with a RAS mutation, especially when combined with oxaliplatin [I/A]."

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9. (eUpdate: 20 September 2016; Corrigendum: 21 July 2015)]



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:

- "It has been demonstrated that the (potential) benefit of anti-EGFR antibodies in all treatment lines and either as a single agent or in combination with any chemotherapy regimen is limited to patients in whom a RAS mutation is excluded. It was shown that the 'expanded RAS' analysis (also including the detection of mutations in exons 3 and 4 of the KRAS gene as well as mutations in the NRAS [exons 2-4] gene) is superior to the KRAS (exon 2) analysis in predicting both more efficacy in the expanded RAS wild-type (WT) patients and a potential detrimental effect in patients harbouring any RAS mutation in their tumour genome [II/A]."

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9. (eUpdate: 20 September 2016; Corrigendum: 21 July 2015)]

⊘ panitumumab + chemotherapy

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

- "It has been demonstrated that the (potential) benefit of anti-EGFR antibodies in all treatment lines and either as a single agent or in combination with any chemotherapy regimen is limited to patients in whom a RAS mutation is excluded. It was shown that the 'expanded RAS' analysis (also including the detection of mutations in exons 3 and 4 of the KRAS gene as well as mutations in the NRAS [exons 2-4] gene) is superior to the KRAS (exon 2) analysis in predicting both more efficacy in the expanded RAS wild-type (WT) patients and a potential detrimental effect in patients harbouring any RAS mutation in their tumour genome [II/A]."
- "Thus, the activity of the anti-EGFR antibodies is confined to RAS WT tumours (and not only KRAS WT tumours). This is true for the combinations of cetuximab or panitumumab alone or with irinotecan- and oxaliplatin-based regimens. Treatment with anti-EGFR antibodies may even harm patients with a RAS mutation, especially when combined with oxaliplatin [I/A]."

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9. (eUpdate: 20 September 2016; Corrigendum: 21 July 2015)]



Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



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