



Com|Pl|i|t DX

SAMPLE INFORMATION

Name	-	Date Sp. Extracted	-
ID/Medical ID	-	Req. Physician	-
Date of Birth	-	Report No	26xxxxxxGR
Material #1	PARAFFIN EMBEDDED TISSUE-BLOCK	Date Received	-
Material #2	-	Date of Report	-
Sample #1 ID	-	Tumor type	Colon Cancer

Com.PL.i.t. Dx (77 genes, 19 fusions) | Comprehensive Panel for Individualized Treatment

1. Clinically Significant Biomarkers*

Biomarker	Result	Therapies with strong clinical significance		Therapies with potential significance	Therapies with potential resistance
		Approved/ Standard of care therapies (Level A)	Therapies in well powered studies (Level B)	Off label/ Investigational therapies (Level C)	
KRAS	Exon 2 p.G12D VAF: 9%	-	-	Avutometinib+Defactinib	Cetuximab Tucatinib+Trastuzumab Panitumumab
Microsatellite Instability (MSI)	Stable (MSS)	-	-	-	-
Immunohistochemistry Biomarkers					
HER2 expression (IHC) (Table S1)	Negative (Score 0)	-	-	-	-

In the Adjuvant/Neoadjuvant setting for colon and rectal cancers consider the following biomarkers for possible treatment: dMMR/MSI-H, POLE/ POLD1 and PIK3CA. For all other findings, there are currently no approved therapies or established guidelines for patients with early-stage disease. However, these findings may become clinically relevant in the event of disease relapse or progression to metastatic disease.

*Note: Variants' Level of Evidence (LoE) (e.g. A, B, C etc) are based on the Joint consensus recommendation of AMP, ACMG, ASCO and CAP for reporting genetic variants in cancer. For a detailed description of the recommendation please refer to Fig. 1

^ The analysis of selected biomarkers included in the present multigene panel is performed within the scope of accreditation according to ELOT EN ISO 15189:2022 (see «Methodology» section). Accreditation according to ELOT EN ISO 15189:2022 applies exclusively to the analytical determination of the selected biomarkers. Interpretations related to the prediction of therapeutic response are not included in the scope of accreditation.



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2. Methodology

NGS analysis

DNA is extracted from the sample under investigation using the Qiamp DNA FFPE Kit (Qiagen). RNA was extracted using the RNeasy FFPE Kit (Qiagen). A total of 83 unique genes is analyzed, including the entire coding sequences of 77 genes and 19 RNA fusions, using the Pan Cancer Panel NGS Assay (Genes2Me). This is a CE-IVD hybrid capture–based assay, in which target genomic regions are enriched through probe hybridization technology. The assay enables the detection of single nucleotide variants (SNVs), insertions/deletions (indels), copy number variations (CNVs), and RNA fusions (Table 1).

Sequencing is performed on the DNBSEQ-T7 next-generation sequencing platform (MGI). Raw sequencing data are processed and analyzed using the CliSeq Interpreter, a companion software for automated, cloud-based analysis. In addition, the SeqPilot software (Version 4.4, Build 505; JSI Medical Systems) is used for independent variant calling and result confirmation.

Alteration- and tumor type-specific therapeutic implications are classified using the OncoKB™ Levels of Evidence system, which assigns clinical actionability to individual mutational events. For additional details about the OncoKB™ curation process, please refer to the version-controlled OncoKB™ Curation Standard Operating Procedure.

Genes Analyzed

77 Gene Alterations									
ABL1	AKT1	ALK	APC	ARAF	ATM	BRAF*	BRCA2*	CCNE1*	CDH1
CDKN2A*	CSF1R	CTNNB1	DDR2	DICER1	EGFR*	EIF1AX	ERBB2*	ERBB3	ERBB4
EZH2	FBXW7	FGFR1*	FGFR2*	FGFR3	FLT3	FOXL2	GNA11	GNAQ	GNAS
HGF	HNF1A	HRAS	IDH1	IDH2	JAK2	JAK3	KDR	KEAP1	KIT
KRAS	LAG3	MAP2K1	MDM2	MET*	MLH1*	MPL	MTAP*	MYC	NOTCH1
NPM1	NRAS	NTRK1	NTRK2	NTRK3	PDGFRA	PIK3CA	PIK3R1	POLD1	POLE
PTEN*	PTPN11	RAC1	RAF1	RB1	RET	ROS1	SMAD4	SMARCA4*	SMARCB1
SMO	SPOP	STK11	SRC	TERT	TP53	VHL			
19 Fusion Genes									
ALK	BRAF	EGFR	ERG	FGFR1	FGFR2	FGFR3	MET	NRG1	NTRK1
NTRK2	NTRK3	PBX1	PPARG	PRKACA	RAF1	RET	ROS1	TFE3	

*CNV (amplification/deletion) analysis is included for these genes





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Biomarkers within the scope of accreditation (ISO15189:2022)

-AKT1, EGFR, ERBB2, KRAS, NRAS, METex14 skipping HRAS, IDH1, IDH2, KIT, PIK3CA, PDGFRA (SNV/indel detection by NGS)

-ALK, ROS1, RET, FGFR1,2,3, NTRK1,2,3, METex14 skipping (Fusion detection by NGS)

-MSI (HRM Real-time PCR)

-PDL1 SP263 & SP142 (IHC)

-ALK (FISH)

-HER2 (IHC, FISH, DISH)

Sensitivity: Positive reference standards are tested with the assay, all corresponding mutation sites can be accurately detected, and the positive percent agreement (PPA) for all variants (SNVs, Indels, fusions and CNVs) assessed was 100%.

Specificity: Negative reference standards are tested with the assay, and the negative percent agreement (NPA) of SNVs, Indels, fusions and CNVs was 100%.

Limit of Detection (LoD): The limit of detection (LoD) of this assay is listed in the table below. The LoD is based on as low as 50 ng of gDNA input for library preparation. The assay can also be used to test microsatellite instability (MSI) with a tumor cell content as low as 10%.

The performance characteristics of the assay are summarized in the following table:

Feature	Performance
Precision (%)	>96
Reproducibility (%)	97
On-Target Ratio (%)	85–95
Analytical Sensitivity (%)	96
Analytical Specificity (%)	100
Repeatability (%)	96
Limit of Detection (LoD, VAF)	≥ 1%

Disclaimer

1. This test is mainly used to assist clinical decision-making, and the result does not represent clinical decision.
2. The test should be interpreted by combining the actual patient context. The medication information provided only on the basis of genetic test results, and the actual medication should follow the physician's instructions.
3. The clinical trials only present partial relevant clinical recruitment trials. For more comprehensive and updated information, please refer to the website: <https://clinicaltrials.gov/>.
4. As evidence on variants and drugs evolves, previous classifications may later be modified. The interpretation of a variant is based on current available evidence.



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5. Sequence variants were reported using Human Genome Variation Society (HGVS) nomenclature. Classification and interpretation of variants follow guidelines of American College of Medical Genetics and Genomics (ACMG), Association of Molecular Pathology (AMP), American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP).
6. Database and references used: Reference genome (GRCh37), annotation using A Locus Reference Genomic (LRG), database referencing 1000G (phaseIII-ucsc), EXAC (0.3.1), dbSNP (147), PolyPhen2/SIFT (ensdb v73), PhyloP (2013-12-06), Clinvar (2018-8) and Cosmic(V80).

Limitations

1. Limited tissue detection may not represent the whole DNA variations of lesions because of tumor heterogeneity.
2. Scientific data show that not all patients carry genomic variations that are associated with targeted drug, therefore not all subjects can be matched with targeted therapies or clear resistance mechanism.
3. Genetic variation beyond the detection range of this test or some non-gene mutation related factors such as drug interactions may affect the clinical effects of drugs.
4. The detection method cannot distinguish between somatic mutations and germline mutations effectively without control sample analysis.
5. Every molecular test has an internal 0.5-1% chance of failure. This is due to rare molecular events and factors related to the preparation and analysis of the samples.
6. Improper sample collection, transportation and storage may lead to compromised or invalid results.



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3. Quality Control Results

Quality Control Index	Result	Criterion
Average effective sequencing depth ¹	598	≥ 500
Tumor cell content ²	20%	≥20%
Overall Assessment ³	PASS	

Note :

1. Average effective sequencing depth: Average sequencing depth on target without duplicated reads.
2. An overall tumor cell content percentage of $\geq 20\%$ is recommended for the efficient detection of somatic alterations in the sample analyzed.
3. Overall Assessment: The quality control overall assessment results are divided into two levels: "PASS" and "RISK". When the overall quality assessment result is "RISK", 94-96% of coverage was achieved in the genes analysed, hence there is a small range where clinical actionable variations could be undetected.

Microsatellite instability

Genomic DNA was extracted from the examined formalin-fixed, paraffin-embedded (FFPE) tumor tissue sample. Assessment of microsatellite instability (MSI) was performed using the MicroSight MSI - 1-step HRM Analysis method, which is based on real-time PCR followed by high-resolution melting (HRM) curve analysis.

The test targets five mononucleotide microsatellite markers (BAT25, BAT26, NR22, NR24, and MONO27), known for their high sensitivity in MSI detection. Differences are detected using specific fluorescent EasyBeacon probes with Intercalating Nucleic Acid (INA) technology, which enhances specificity and curve resolution during melting analysis.

Interpretation is based on comparing the melting profile of the tumor sample to a predefined universal reference DNA. Each microsatellite marker is classified as either stable (MSS) or unstable (MSI-H), and the overall classification of the sample depends on the number of unstable markers:

- Sample with 0-2 unstable markers: classified as microsatellite stable (MSS)
- Sample with ≥ 3 unstable markers ($\geq 60\%$): classified as microsatellite instability-high (MSI-H).



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ERBB2 (HER2) expression by IHC

ERBB2 staining is performed in a VENTANA BenchMark Series automated staining instrument using the ERBB2 clone 4B5, on formalin-fixed, paraffin-embedded (FFPE) tissue. The IHC test gives a score of 0 to 3+ that measures the amount of HER2 receptor protein on the surface of cancer cells. Scoring interpretation is as follows:

HER2 IHC positive (score 3+)

HER2 IHC equivocal (score 2+)

HER2 IHC negative (score 0 or 1+)

Scoring is based on the ASCO-CAP HER2 testing guidelines (PMID: [27841667](#), [37303228](#)).

For mCRC the HERACLES criteria are also used (PMID: [26449765](#)).



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4. Important biomarkers findings

Gene	Finding (VAF)	Gene	Finding (VAF)
KRAS	p.G12D (9%)	ERBB2 amplification	Not Detected
NRAS	Not Detected	MSI status	MSS
BRAF_V600E	Not Detected	NTRK1/2/3 rearrangement	Not Detected

5. Immune Checkpoint inhibitors biomarkers

Biomarker/Variant	Result	Clinical Interpretation
Treatment effect - positive correlation		
MSI status	MSS	-
POLE mutation (driver)	Not Detected	-
TP53 mutation	Not Detected	-
KRAS mutation	Detected	May increase the benefit rate of PD-1/PD-L1 inhibitors
Treatment effect - negative correlation		
PTEN inactivating mutation	Not Detected	-
JAK2 inactivating mutation	Not Detected	-
EGFR mutation (L858R/EX19del)	Not Detected	-
ALK rearrangement	Not Detected	-
STK11 inactivating mutation	Not Detected	-
KEAP1 inactivating mutation	Not Detected	-
MDM2 amplification	Not Detected	-



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6. Interpretations for targeted therapies

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

VAF*: 9%

OncoKB

Treatment Information

The presence of KRAS mutations is associated with a high likelihood of resistance to therapies targeting EGFR (Panitumumab, Cetuximab) (PMID: [18202412](#), [24024839](#), [18316791](#)). According to MOUNTAINEER clinical trial, KRAS and NRAS mutations may confer resistance to the anti-HER2 therapy Tucatinib & Trastuzumab. To date, most efforts to treat cancers with RAS mutations have focused on targeting downstream effectors of mutant RAS, such as RAF, MEK, or PI3K, each of which is druggable. MEK inhibitors have been the most widely investigated, typically as a combination therapy, despite the presence of multiple inhibitors that are being explored to target different KRAS-activated pathways. In the IMblaze370 trial, which evaluated Atezolizumab alone and in combination with Cobimetinib against monotherapy use of Regorafenib, the combination did not demonstrate improved overall survival (PMID: [31003911](#)). Currently, there are no other clinical trials including cobimetinib for colorectal cancer. The MEK inhibitor binimetinib is being examined in a number of clinical trials for patients with KRAS-mutated colorectal cancer, including studies looking at the agent in combination with mFOLFIRIL (NCT02613650) and with palbociclib (NCT03981614). Clinical trials evaluating the efficacy of trametinib, a potent MEK inhibitor clinically approved for BRAF mutant cancers (mainly melanoma), in colorectal cancer have been conducted (NCT03317119, NCT03668431, NCT03714958, NCT04111458). Avutometinib is an inhibitor of Ras-Raf-MEK-ERK signaling being developed as a potential treatment for cancer. Defactinib is a small-molecule, oral focal adhesion kinase (FAK) inhibitor. It works by blocking FAK, a tyrosine kinase involved in cell adhesion and signaling pathways, including RAS/MEK/ERK and PI3K/Akt. Defactinib has been studied in various clinical trials for its potential anti-tumor and anti-angiogenic activities. In 2025 FDA approved defactinib in combination with avutometinib for the treatment of adult patients with recurrent low-grade serous ovarian cancer. A phase I clinical trial of RMC-6236 in patients with advanced refractory solid cancers harboring specific KRAS mutations (G12A, G12D, G12R, G12S, G12V) is ongoing (NCT05379985). Finally, a phase I/II trial of SX-628 (CXCR1/2 inhibitor) in combination with nivolumab is ongoing in refractory RAS mutant, MSS CRC (NCT04599140). Efforts to induce an immune response against these tumors are under investigation (PMID: [36638742](#)).

Gene information

KRAS is a member of the RAS family of small GTPases, which catalyze the hydrolysis of GTP to GDP. Under physiologic conditions, these RAS proteins cycle between an active (GTP-bound) and an inactive (GDP-bound) state, to activate the MAPK and PI3K oncogenic pathway signaling downstream of Receptor Tyrosine Kinases (RTKs) (PMID: [22189424](#)). The function of RAS enzymes is regulated by guanine nucleotide exchange factors (GEFs), such as SOS, which enable the exchange of GDP to GTP, as well as by GTPase activating proteins, such as NF1, which increase the ability of RAS to hydrolyze GTP. Once activated, RAS mediates the regulation of cellular proliferation and other cellular functions through the activation of distinct intracellular signaling pathways, including the RAF/MEK/ERK and PI3K/AKT/mTOR pathways. Transforming mutations in KRAS are frequently found in pancreatic, colon, endometrial, ovarian and biliary cancers; almost all of these mutations result in constitutive activation of KRAS, thereby promoting cell proliferation (PMID: [21993244](#), [24651010](#)). KRAS mutations occur primarily in three major hotspots, G12, G13 and Q61, the first two of which occur in the GTP-ase domain and the latter interferes with the ability of NF1 to bind and regulate KRAS (PMID: [22589270](#), [21993244](#), [24651010](#)). Other less well-characterized mutations such as A146T/V/P and L19F have also been characterized and found to be activating albeit at lower frequencies (PMID: [20147967](#), [20432530](#), [20570890](#)). Germline KRAS mutations are responsible for both Noonan syndrome (NS)



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and cardio-facio-cutaneous (CFC) syndrome (PMID: [16474405](#), [16474404](#), [19467855](#), [17056636](#)) that are associated with hyperactivated MAPK pathway, distinctive clinical characteristics and a predisposition to cancer (PMID: [19467855](#), [17704260](#)).

Variant Information

The KRAS G12D mutation is known to be oncogenic. The KRAS G12D mutation is located in the P-loop of the catalytic G-domain of the protein. This mutation has been found in lung, colorectal, pancreatic and ovarian cancer (PMID: [28572459](#)). Expression of this mutation in cell lines and mouse models demonstrated that it is activating, as measured by increased downstream pathway activation, colony formation and in vivo tumor development across multiple lineages compared to wildtype (PMID: [20570890](#), [20147967](#), [11751631](#), [15093544](#), [19296721](#), [17349581](#), [32792368](#)). In vitro studies have demonstrated that this mutation confers resistance to BRAF inhibition in lymphoid cells as measured by decreased pathway activation in the presence of the drug, but is sensitive to the MEK inhibitor cobimetinib (PMID: [30341394](#)). A patient with hairy cell leukemia acquired a KRAS G12D mutation following relapse on the BRAF inhibitor vemurafenib but was successfully treated with the cobimetinib for at least twelve months (PMID: [30341394](#)). Preclinical studies with xenograft mouse models expressing KRAS G12D demonstrated sensitivity to treatment with setidegrasib as measured by reduced tumor volume following treatment (Abstract: Nagashima et al. Abstract# 5735, AACR 2023.).

Cetuximab

DrugBank

Cetuximab and panitumumab are anti-EGFR monoclonal antibodies that are FDA-approved for patients with EGFR expressing, RAS-wildtype colorectal cancer. Patients with metastatic colorectal cancer (mCRC) harboring either exon 2 (e.g. G12, G13) or non-exon 2 (e.g. Q61, K117, A146) KRAS mutations do not respond favorably to the anti-EGFR therapies cetuximab (PMID: [21228335](#), [20619739](#)) or panitumumab (PMID: [18316791](#), [20921465](#), [24024839](#)).

Tucatinib+Trastuzumab

DrugBank

Tucatinib, a small molecular inhibitor of HER2, and trastuzumab, a HER2-targeted antibody, are FDA-approved in combination for the treatment of patients with HER2 amplified metastatic colorectal cancer whose tumors are also RAS and BRAF wildtype. Patients with metastatic colorectal cancer harboring KRAS mutations do not respond favorably to trastuzumab as seen in the MyPath trial. In the multiple basket MyPath Phase IIa trial of pertuzumab and trastuzumab in which 56 metastatic colorectal cancer patients with HER2 amplification received combination therapy, the objective response rate for patients with KRAS wildtype colorectal cancer (43/56 patients) compared to KRAS mutated colorectal cancer (13/56 patients) was 40% (17/43, 95% CI, 25%–56%) versus 8% (1/13, 95% CI 0.2%–36%), respectively (PMID: [30857956](#)).

Panitumumab

DrugBank

Cetuximab and panitumumab are anti-EGFR monoclonal antibodies that are FDA-approved for patients with EGFR expressing, RAS-wildtype colorectal cancer. Patients with metastatic colorectal cancer (mCRC) harboring either exon 2 (e.g. G12, G13) or non-exon 2 (e.g. Q61, K117, A146) KRAS mutations do not respond favorably to the anti-EGFR therapies cetuximab (PMID: [21228335](#), [20619739](#)) or panitumumab (PMID: [18316791](#), [20921465](#), [24024839](#)).



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Avutometinib+Defactinib

DrugBank

Avutometinib, a RAF/MEK clamp inhibitor, and defactinib, a FAK inhibitor, are FDA-approved in combination for the treatment of adult patients with KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC) who have received prior systemic therapy. FDA approval was based on the results of the Phase II RAMP-201 (NCT04625270) trial of avutometinib plus defactinib in 109 patients with recurrent LGSOC.

In the Phase II RAMP-201 (NCT04625270) trial, patients with KRAS-mutated LGSOC (n=57) demonstrated an overall response rate (ORR) of 44% (n=25), with a 2% (n=2) complete response (CR) rate, 40% (n=23) partial response (PR) rate and 49% (n=28) stable disease (SD) rate, a median duration of response (DOR) of 31.0 months (95% CI=14.8-31.1) and a median progression-free survival (PFS) of 22.0 months (95% CI=11.1-36.6) (PMID: [40644648](#)). Responders included patients with the following KRAS mutations: KRAS A146V, G12D, G12R, G12V and Q61H (PMID: [40644648](#)). Of patients with KRAS wildtype LGSOC (n=52), the cohort demonstrated an ORR of 17% (n=9), with a 17% (n=9) PR rate and 65% (n=34) SD rate, and a median PFS of 9.2 months (95% CI=5.5-NE) (PMID: [40644648](#)).

*VAF: Variant Allele Frequency



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7. Clinical Trials to consider

KRAS associated clinical trials

[NCT05797467](#)

PHASE3

Title	Adjuvant Chemotherapy Combined With Targeted Therapy or Not in the T3-4N2 Colorectal Cancer Patients
Treatment	FOLFOX chemotherapy regimens Bevacizumab
Location	China

[NCT06555003](#)

PHASE3

Title	DEBIRI Plus Chemotherapy vs. Chemotherapy Alone in Colorectal Cancer Liver Metastases
Treatment	Drug-Eluting Embolic Bead Chemotherapy drug
Location	Iran

[NCT06973564](#)

PHASE1 | PHASE2

Title	JAB-23E73 in Adult Participants With Advanced Solid Tumors With KRAS Alteration
Treatment	JAB-23E73 JAB-23E73 JAB-23E73
Location	United States

[NCT06575127](#)

PHASE2

Title	Modified FOLFOXIRI Plus Target Therapy as a First Line Treatment for Advanced Colorectal Cancer a Prospective Phase Two Study
Treatment	FOLFOXIRI Protocol
Location	Egypt

[NCT05327010](#)

PHASE2

Title	Testing the Combination of the Anti-cancer Drugs ZEN003694 (ZEN-3694) and Talazoparib in Patients With Advanced Solid Tumors, The ComBET Trial
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Name	-	Report No	26xxxxxxGR
Treatment	BET Bromodomain Inhibitor ZEN-3694 Biopsy Procedure Biospecimen Collection Diagnostic Imaging Testing Talazoparib		
Location	United States		

NCT06229340		PHASE2
Title	Leflunomide or Combination of MEK Inhibitor and Hydroxychloroquine for Refractory Patients With RAS Mutations	
Treatment	Leflunomide The combination of MEK inhibitor + hydroxychloroquine(plaquenil) ± bevacizumab	
Location	Russia	

NCT06520488		PHASE1 PHASE2
Title	A Study of HRS-4642 in Combination With Antineoplastic Agents in Advanced Solid Tumors	
Treatment	HRS-4642	
Location	China	

NCT06949982		PHASE2
Title	Efficacy And Safety Of Hydroxychloroquine Combined With Methotrexate, Capecitabine And Bevacizumab Vs. Regorafenib In Participants With Refractory Metastatic Colorectal Cancer With Mutations In RAS Genes	
Treatment	experimental group x-MAP Regorafenib (BAY 73-4506)	
Location	Russia	

NCT06934538		PHASE1 PHASE2
Title	First-in-human Trial of STC-1010, an Immunotherapy, in Patients With Unresectable Locally Advanced or Metastatic Colorectal Cancer	
Treatment	STC-1010 + IS regimen + SOC therapy	
Location	Belgium, France, United States	

NCT05379985		PHASE1 PHASE2
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Name	-	Report No	26xxxxxxGR
Title	Study of RMC-6236 in Patients With Advanced Solid Tumors Harboring Specific Mutations in RAS		
Treatment	RMC-6236		
Location	United States		

NCT06634875		PHASE2
Title	Isunakinra Alone and in Combination With Pembrolizumab in Patients With Colorectal Cancer (MSS)	
Treatment	isunakinra	
Location	United States	

NCT05786924		PHASE1 PHASE2
Title	Phase 1/2 Trial of S241656 in Selected RAS/MAPK Mutation- Positive Malignancies	
Treatment	S241656 FOLFOX6/FOLFOX7 FOLFIRI Cetuximab Panitumumab Gemcitabine Nab-paclitaxel	
Location	Denmark, Hong Kong, Japan, United Kingdom, United States	

NCT06959615		PHASE1 PHASE2
Title	A Phase I/IIa Study of JAB-23E73 in Patients With Advanced Solid Tumors Harboring KRAS Gene Alteration	
Treatment	JAB-23E73 JAB-23E73	
Location	China	

NCT07223047		PHASE1 PHASE2
Title	A Study to Evaluate the Safety, Tolerability, and Efficacy of BMS-986523 Alone and in Combination With Anti-Cancer Agents in Participants With Advanced Solid Malignancies	
Treatment	BMS-986523 Gemcitabine Nab-Paclitaxel Cetuximab Pembrolizumab	
Location	Canada, Spain, United States	

NCT06947811		PHASE1 PHASE2
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Name	-	Report No	26xxxxxxGR
Title	A Study of Almonertinib Combined With Palbociclib in Patients With Advanced Solid Tumors Harboring KRAS Mutations		
Treatment	Almonertinib Palbociclib		
Location	China		

NCT06895031		PHASE2
Title	Study of JYP0015 in Patients With Advanced Solid Tumors Harboring Specific Mutations in RAS	
Treatment	JYP0015	
Location	China	

NCT02029001		PHASE2
Title	Adapting Treatment to the Tumor Molecular Alterations for Patients With Advanced Solid Tumors: MyOwnSpecificTreatment	
Treatment	Nilotinib (400 mg BID) Everolimus (10 mg QD) Sorafenib (400 mg BID) Lapatinib (1500 mg QD) Pazopanib (800 mg QD) Olaparib (300 mg BID) Durvalumab + Tremelimumab	
Location	France	

NCT07148128		PHASE1 PHASE2
Title	Phase 1/2a Study to Assess the Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of WEF-001 as Monotherapy in Advanced KRAS-Mutant Solid Tumours.	
Treatment	WEF-001	
Location	Canada, United Kingdom, United States	

NCT06243354		PHASE1 PHASE2
Title	Phase 1/2 Study of HYP-2090PTSA in Patients With Advanced Solid Tumors Harboring KRAS Mutation	
Treatment	Test product: HYP-2090PTSA	
Location	China	



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Name		Report No	26xxxxxxGR
NCT06026410			PHASE1
Title	KO-2806 Monotherapy and Combination Therapies in Advanced Solid Tumors		
Treatment	Darlifarnib Cabozantinib Adagrasib		
Location	France, Germany, Italy, Spain, United States		

NCT06619587		PHASE1
Title	A Study to Evaluate Safety, Pharmacokinetics, and Activity of GDC-7035 as a Single Agent and in Combination in Patients With Advanced Solid Tumors	
Treatment	Phase I Arm A Phase I Arm B	
Location	Australia, Canada, France, Israel, Singapore, South Korea, Spain, United Kingdom, United States	

NCT07094113		PHASE1
Title	AMG 410 Alone and in Combination With Other Agents in Participants With KRAS Altered Advanced or Metastatic Solid Tumors	
Treatment	AMG 410 Pembrolizumab Panitumumab	
Location	Australia, Belgium, Canada, China, Denmark, France, Germany, Italy, Japan, Netherlands, South Korea, Spain, United Kingdom, United States	

NCT07207707		PHASE1
Title	A Study to Investigate the Safety and Efficacy of KQB548 in Participants With Advanced Solid Malignancies	
Treatment	KQB548	
Location	United States	

NCT05067283		PHASE1
Title	A Study of Caldesasib (MK-1084) in KRAS Mutant Advanced Solid Tumors (MK-1084-001)	
Treatment	Caldesasib Pembrolizumab carboplatin pemetrexed cetuximab oxaliplatin leucovorin 5-fluorouracil	



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Name	-	Report No	26xxxxxxGR
Location	Argentina, Australia, Canada, Chile, China, Denmark, Israel, Italy, Japan, Lithuania, Malaysia, New Zealand, Panama, Poland, South Korea, Spain, Switzerland, Taiwan, Turkey (Türkiye), Ukraine, United States		

NCT06962254		PHASE1
Title	Imatinib and Trametinib for KRAS-mutated Solid Tumor	
Treatment	Imatinib Trametinib	
Location	Taiwan	

NCT07300150		PHASE1
Title	A Study of PT0511 in Participants With KRAS Mutated or Amplified Advanced Solid Tumors	
Treatment	PT0511 Cetuximab	
Location	South Korea, United States	

NCT06484790		PHASE1
Title	T Cell Receptor Gene-Engineered T Cell Therapy Targeting KRAS Mutations in the Treatment of Subjects With Advanced Solid Tumor	
Treatment	NW-301V NW-301D	
Location	China	

NCT05438667		EARLY_PHASE1
Title	TCR-T Cell Therapy on Advanced Solid Tumors	
Treatment	TCR-T therapy	
Location	China	

NCT06336902		PHASE1
Title	Botensilimab Plus Balstilimab and Fasting Mimicking Diet Plus Vitamin C for Patients With KRAS-Mutant Metastatic Colorectal Cancer	



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Name	-	Report No	26xxxxxxGR
Treatment	Balstilimab Biospecimen Collection Botensilimab Computed Tomography Dietary Intervention Magnetic Resonance Imaging Vitamin C		
Location	United States		

NCT07094204		PHASE1
Title	A Study to Find a Suitable Dose of ASP5834 in Adults With Solid Tumors	
Treatment	ASP5834 panitumumab	
Location	France, Japan, Spain, United States	

NCT06835569		PHASE1
Title	A Study to Learn About Study Medicine ALTA3263 in Adults With Advanced Solid Tumors With KRAS Mutations	
Treatment	ALTA3263 cetuximab mFOLFOX6 Pembrolizumab Pemetrexed + Cisplatin /Carboplatin mFOLFIRINOX GnP Midazolam	
Location	United States	

NCT06478251		PHASE1
Title	T Cell Receptor Gene-Engineered T Cell Therapy Targeting KRAS Mutations in the Treatment of Subjects With Advanced Solid Tumor	
Treatment	NW-301V NW-301D	
Location	China	

NCT06577532		EARLY_PHASE1
Title	Study of KRAS Neoantigen mRNA Vaccine (ABO2102) in Patients With KRAS -Mutated Solid Tumors	
Treatment	ABO2102 Toripalimab	
Location	China	

NCT06625775		PHASE1
Title	Open-Label Study of BBO-10203 in Subjects With Advanced Solid Tumors	



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Name	-	Report No	26xxxxxxGR
Treatment	BBO-10203 Trastuzumab Fulvestrant Ribociclib FOLFOX Bevacizumab		
Location	Australia, Brazil, France, Spain, United States		

NCT07021898		PHASE1
Title	A Study of ERAS-4001 in Patients With Advanced or Metastatic Solid Tumors.	
Treatment	ERAS-4001 ERAS-4001 in combination	
Location	United States	

NCT06096974		PHASE1
Title	Pan-RAS Inhibitor YL-17231 in Patients With Advanced Solid Tumors Harboring Mutations in KRAS, HRAS, or NRAS	
Treatment	YL-17231	
Location	United States	

NCT07204340		PHASE1
Title	TLN-372 in Advanced KRAS Mutant Solid Tumors	
Treatment	TLN-372 TLN-372 in combination with cetuximab TLN-372 in combination with pembrolizumab	
Location	Australia, Canada, Spain, United States	

NCT06403735		PHASE1
Title	A Phase I Clinical Study of QLC1101 in Patients With Advanced Solid Tumors	
Treatment	QLC1101	
Location	China	

NCT06944457		PHASE1
Title	Clinical Trial to Evaluate the Safety, Tolerability and Pharmacokinetics of MPD-1 in Patients With Advanced Solid Tumor	
Treatment	MPD-1	



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Name	-	Report No	26xxxxxxGR
Location	South Korea		

NCT06487377		PHASE1
Title	IX001 TCR-T In the Treatment of Advanced Pancreatic Cancer and Colorectal Cancer Induced by KRAS Mutations	
Treatment	IX001 TCR-T cells	
Location	China	

NCT06804824		PHASE1
Title	A First-in-Human (FIH) Study to Evaluate the Safety and Tolerability of VVD-159642 in Participants With Advanced Solid Tumors	
Treatment	VVD-159642 Sotorasib Trametinib	
Location	Australia, United States	

NCT05382559		PHASE1
Title	A Study of ASP3082 in Adults With Advanced Solid Tumors	
Treatment	Setidegrasib Cetuximab Leucovorin Oxaliplatin Fluorouracil Irinotecan Nanoparticle albumin-bound-paclitaxel Gemcitabine Docetaxel Pembrolizumab Cisplatin Carboplatin Pemetrexed Liposomal Irinotecan	
Location	China, France, Japan, Puerto Rico, South Korea, Spain, United States	

NCT06218914		PHASE1
Title	Phase 1 Study to Investigate TCRTs KRAS Mutation in Unresectable, Advanced, and/or Metastatic Solid Tumors	
Treatment	NT-112: Autologous, engineered T Cells targeting KRAS G12D AZD0240: Autologous, engineered T Cells targeting KRAS G12D	
Location	United States	

NCT06917079		PHASE1
Title	BBO-11818 in Adult Subjects With KRAS Mutant Cancer	



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Name	-	Report No	26xxxxxxGR
Treatment	BBO-11818 Pembrolizumab Platinum chemotherapy (cisplatin or carboplatin) Pemetrexed Cetuximab mFOLFOX6 mFOLFOX6 BBO-10203 mFOLFIRINOX Gemcitabine Nab-paclitaxel		
Location	Australia, United States		

NCT06484556		PHASE1
Title	T Cell Receptor Gene-Engineered T Cell Therapy Targeting KRAS Mutations in the Treatment of Subjects With Advanced Solid Tumor	
Treatment	NW-301V NW-301D	
Location	China	

NCT05661201		PHASE1
Title	NEROFE and Doxorubicin in KRAS-mutated ST2-positive Solid Tumors	
Treatment	NEROFE Doxorubicin	
Location	United States	

Press [here](#) for a live search of clinical trials for KRAS



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8. Appendix

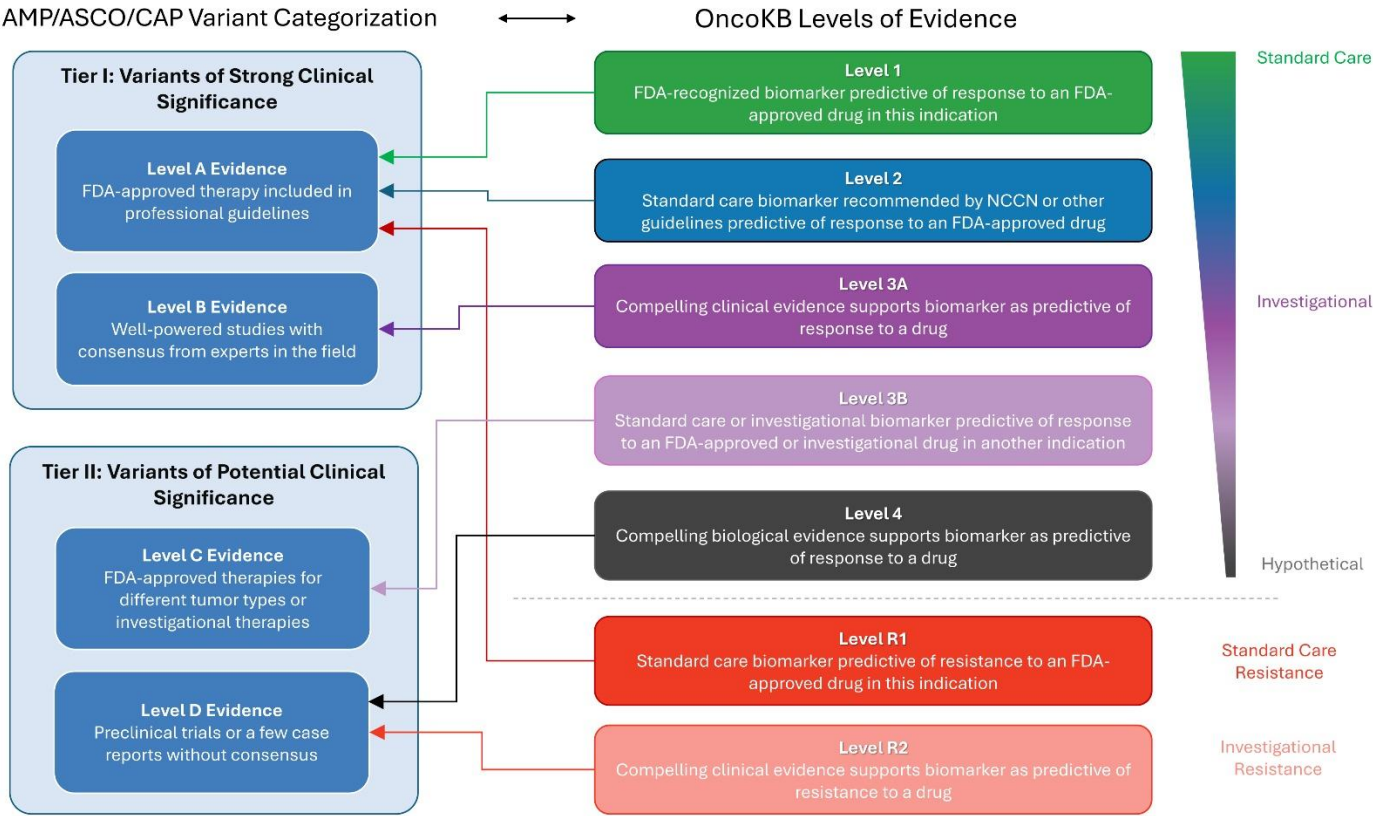


Figure 1. Joint consensus recommendation of AMP, ACMG, ASCO and CAP for reporting genetic variants in cancer. [1-2]

1. Li MM, Datto M, Duncavage EJ, et al. J Mol Diagn. 2017 Jan;19(1):4-23.
2. Leichsenring J, Horak P, Kreutzfeldt S, et al. Int J Cancer. 2019 Dec 1;145(11):2996-3010.

ERBB2 (HER2) expression by IHC

ERBB2, a receptor tyrosine kinase, is altered by mutation, amplification and/or overexpression in various cancer types, most frequently in breast, esophagogastric and endometrial cancers. FDA has granted approval to several anti-ERBB2 regimens, either as single or combination therapy for various cancer types. In addition, recently FDA granted accelerated approval to fam-trastuzumab deruxtecan-nxki, for adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.



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Table S1. ERBB2 Biomarkers associated with treatment response (LoE)

Cancer Type	3+ IHC	2+ IHC & ≥2 FISH	ERBB2 amplification by NGS	IHC 1+ or IHC 2+/ISH -ve
Breast Cancer	<u>Trastuzumab Deruxtecan</u> (1A.1) <u>Trastuzumab</u> (1A.1) <u>Ado-Trastuzumab Emtansine</u> (1A.1) <u>Lapatinib + Capecitabine</u> (1A.1) <u>Lapatinib + Letrozole</u> (1A.1) <u>Margetuximab + Chemotherapy</u> (1A.1) <u>Neratinib</u> (1A.1) <u>Neratinib + Capecitabine</u> (1A.1) <u>Trastuzumab + Tucatinib + Capecitabine</u> (1A.1) <u>Trastuzumab + Chemotherapy</u> (1A.1) <u>Trastuzumab + Pertuzumab + Chemotherapy</u> (1A.1)	<u>Trastuzumab Deruxtecan</u> (1A.1) <u>Ado-Trastuzumab Emtansine</u> (1A.1) <u>Lapatinib + Capecitabine</u> (1A.1) <u>Lapatinib + Letrozole</u> (1A.1) <u>Margetuximab + Chemotherapy</u> (1A.1) <u>Neratinib</u> (1A.1) <u>Neratinib + Capecitabine</u> (1A.1) <u>Trastuzumab + Tucatinib + Capecitabine</u> (1A.1) <u>Trastuzumab + Chemotherapy</u> (1A.1) <u>Trastuzumab + Pertuzumab + Chemotherapy</u> (1A.1) <u>Trastuzumab</u> (2C.1)	<u>Trastuzumab Deruxtecan</u> (2C.1) <u>Trastuzumab</u> (2C.1) <u>Ado-Trastuzumab Emtansine</u> (2C.1) <u>Lapatinib + Capecitabine</u> (2C.1) <u>Lapatinib + Letrozole</u> (2C.1) <u>Margetuximab + Chemotherapy</u> (2C.1) <u>Neratinib</u> (2C.1) <u>Neratinib + Capecitabine</u> (2C.1) <u>Trastuzumab + Tucatinib + Capecitabine</u> (2C.1) <u>Trastuzumab + Chemotherapy</u> (2C.1) <u>Trastuzumab + Pertuzumab + Chemotherapy</u> (2C.1)	<u>Trastuzumab Deruxtecan</u> (1A.1)
Colorectal Cancer	<u>Trastuzumab Deruxtecan</u> (1A.1) <u>Tucatinib + Trastuzumab</u> (1A.1) <u>Lapatinib + Trastuzumab</u> (1A.2) <u>Trastuzumab + Pertuzumab</u> (1A.2)	<u>Tucatinib + Trastuzumab</u> (1A.1) <u>Lapatinib + Trastuzumab</u> (1A.2) <u>Trastuzumab + Pertuzumab</u> (1A.2) <u>Trastuzumab Deruxtecan</u> (2C.1)	<u>Tucatinib + Trastuzumab</u> (1A.1) (RAS/BRAF wild type) <u>Trastuzumab Deruxtecan</u> (2C.1) <u>Lapatinib + Trastuzumab</u> (2C.1) (RAS/BRAF wild type) <u>Trastuzumab + Pertuzumab</u> (2C.1) (RAS/BRAF wild type)	N/A
Gastric/GEJ	<u>Trastuzumab Deruxtecan</u> (1A.1) <u>Trastuzumab + Chemotherapy</u> (1A.1) <u>Pembrolizumab + Trastuzumab + Chemotherapy</u> (1A.1) (PD-L1 with CPS>1% required) <u>Zanidatamab-hrii + Tislelizumab-jsgr + Chemotherapy</u> (1A.1) <u>Zanidatamab-hrii + Chemotherapy</u> (1A.1)	<u>Pembrolizumab + Trastuzumab + Chemotherapy</u> (1A.1) (PD-L1 with CPS>1% required) <u>Trastuzumab + Chemotherapy</u> (1A.1) <u>Trastuzumab Deruxtecan</u> (1A.1) <u>Zanidatamab-hrii + Tislelizumab-jsgr + Chemotherapy</u> (1A.1)	<u>Pembrolizumab + Trastuzumab + Chemotherapy</u> (2C.1) (PD-L1 with CPS>1% required) <u>Trastuzumab + Chemotherapy</u> (2C.1) <u>Trastuzumab Deruxtecan</u> (2C.1)	N/A
Biliary Tract	<u>Trastuzumab Deruxtecan</u> (1A.1) <u>Zanidatamab-hrii</u> (1A.1) <u>Trastuzumab + Pertuzumab</u> (1A.2) <u>Tucatinib + Trastuzumab</u> (1A.2)	<u>Trastuzumab Deruxtecan</u> (2C.1) <u>Zanidatamab-hrii</u> (2C.1) <u>Trastuzumab + Pertuzumab</u> (1A.2) <u>Tucatinib + Trastuzumab</u> (1A.2)	<u>Trastuzumab Deruxtecan</u> (2C.1) <u>Zanidatamab-hrii</u> (2C.1) <u>Trastuzumab + Pertuzumab</u> (2C.1) <u>Tucatinib + Trastuzumab</u> (2C.1)	N/A
Uterine Serous Carcinoma/ Papillary Serous	<u>Trastuzumab Deruxtecan</u> (1A.1) <u>Trastuzumab + Carboplatin-Taxol Regimen</u> (1A.2)	<u>Trastuzumab Deruxtecan</u> (2C.1) <u>Trastuzumab + Carboplatin-Taxol Regimen</u> (2C.1)	<u>Trastuzumab Deruxtecan</u> (2C.1) <u>Trastuzumab + Carboplatin-Taxol Regimen</u> (2C.1)	N/A



Name		Report No		
-		26xxxxxxGR		
Lung Cancer	Trastuzumab Deruxtecan (1A.1)	Trastuzumab Deruxtecan (2C.1)	Trastuzumab Deruxtecan (2C.1)	N/A
All tumors	Trastuzumab Deruxtecan (1A.1)	Trastuzumab Deruxtecan (2C.1)	Trastuzumab Deruxtecan (2C.1)	N/A



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Microsatellite Instability (MSI)

Microsatellite instability (MSI) is a condition of genetic hypermutability resulting from impaired DNA mismatch repair (MMR) mechanisms. It is characterized by the accumulation of mutations in short repetitive DNA sequences known as microsatellites. MSI-H is found across multiple cancer types, most notably in colorectal, endometrial, gastric, and ovarian cancer. It can arise sporadically or as part of Lynch syndrome, a hereditary condition caused by germline mutations in MMR genes (MLH1, MSH2, MSH6, PMS2).

The results of MSI are divided into three types: MSI-H, which means microsatellites are highly unstable; MSS, which means microsatellites are stable; MSI-U, which means that the sample does not meet the MSI evaluation conditions (tissues or pleural fluid samples may not have passed the MSI indicator calculation quality control due to the low DNA and/or content of tumor cells).

Pembrolizumab has received full FDA approval for adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors (PMID: 35680043, 33264544) — representing the first full approval for an immunotherapy based on a predictive biomarker, regardless of solid tumor type. This approval applies to patients who have progressed after prior treatment and have no satisfactory alternative options. Beyond the tumor-agnostic indication, specific approvals have been granted for tumor types such as endometrial and colorectal cancer.



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9. Biomarker findings across all Levels of evidence (A-D)

Biomarker	Result	Therapies with strong clinical significance		Therapies with potential significance		Therapies with potential resistance
		Approved/ Standard of care therapies (Level A)	Therapies in well powered studies (Level B)	Off label/ Investigational therapies (Level C)	Therapies in pre-clinical trials (Level D)	
KRAS	Exon 2 c.35G>A (p.G12D) VAF: 9%	-	-	Avutometinib+Defactinib	Daraxonrasib MRTX1133 Setidegrasib Trametinib Cobimetinib Binimetinib	Cetuximab Tucatinib+Trastuzumab Panitumumab

10. Treatment Table for Colon and Rectal non metastatic setting based on the NCCN guidelines (acc. June 2025)

Rectal Cancer		
Phase	Indication	Treatment
Neoadjuvant	dMMR/MSI-H or POLE/POLD1 mutation with ultra hypermutated phenotype (e.g., TMB > 50 mut/Mb): - T3, N any - T1-2, N1-2 - T4, N any - Locally unresectable or medically inoperable	Checkpoint inhibitor immunotherapy for up to 6 months: - Dostarlimab-gxly - Nivolumab - Pembrolizumab
Adjuvant	Stage II-III with PIK3CA mutation	Add aspirin 100-162 mg PO daily for 3 years following surgery
Colon Cancer		
Phase	Indication	Treatment
Neoadjuvant	dMMR/MSI-H or POLE/POLD1 mutation with ultra hypermutated phenotype (e.g., TMB > 50 mut/Mb): - Clinical T4b or bulky nodal disease	Consider checkpoint inhibitor immunotherapy (preferred)
	- Locally unresectable or medically inoperable	Checkpoint inhibitor immunotherapy (preferred). Evaluate for complete response or conversion to resectability
Adjuvant	dMMR/MSI-H or POLE/POLD1 mutation with ultra hypermutated phenotype (e.g., TMB > 50 mut/Mb): - Tis, T1-4a, N0, M0 (Stage 0-IIb)	Observation
	- T4b, N0, M0 (Stage IIC)	Observation or consider adjuvant chemotherapy as for low-risk stage III disease
	Stage II-III with PIK3CA mutation	Add aspirin 100-162 mg PO daily for 3 years



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Report No

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11. References

1. Tops BB, Normanno N, Kurth H, Amato E, Mafficini A, Rieber N, Le Corre D, Rachiglio AM, Reiman A, Sheils O, Noppen C, Lacroix L, Cree IA, Scarpa A, Ligtenberg MJ, Laurent-Puig P. Development of a semi-conductor sequencing-based panel for genotyping of colon and lung cancer by the Onconetwork consortium. BMC Cancer. 2015 Jan 31;15:26. doi: 10.1186/s12885-015-1015-5. (PMID: [25637035](#))
2. <https://civic.genome.wustl.edu/>
3. <http://cancer.sanger.ac.uk/>
4. <https://www.clinicaltrials.gov>
5. <http://atlasgeneticsoncology.org>
6. <https://www.oncokb.org/>
7. <https://www.mycancergenome.org/>
8. <https://pmkb.org/>
9. De Roock W, et al. **Effects of KRAS, BRAF, NRAS, and PIK3CA mutations on the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory metastatic colorectal cancer: a retrospective consortium analysis.** Lancet Oncol. 2010; 11:753-62. doi: 10.1016/S1470-2045(10)70130-3 (PMID: [20619739](#))
10. Schubbert S, et al. **Germline KRAS mutations cause Noonan syndrome.** Nat Genet. 2006; 38:331-6. doi: 10.1038/ng1748 (PMID: [16474405](#))
11. Nava C, et al. **Cardio-facio-cutaneous and Noonan syndromes due to mutations in the RAS/MAPK signalling pathway: genotype-phenotype relationships and overlap with Costello syndrome.** J Med Genet. 2007; 44:763-71. doi: 10.1136/jmg.2007.050450 (PMID: [17704260](#))
12. Meric-Bernstam F, et al. **Pertuzumab plus trastuzumab for HER2-amplified metastatic colorectal cancer (MyPathway): an updated report from a multicentre, open-label, phase 2a, multiple basket study.** Lancet Oncol. 2019; 20:518-530. doi: 10.1016/S1470-2045(18)30904-5 (PMID: [30857956](#))
13. Bokemeyer C, et al. **Efficacy according to biomarker status of cetuximab plus FOLFOX-4 as first-line treatment for metastatic colorectal cancer: the OPUS study.** Ann Oncol. 2011; 22:1535-1546. doi: 10.1093/annonc/mdq632 (PMID: [21228335](#))
14. Eng C, et al. **Atezolizumab with or without cobimetinib versus regorafenib in previously treated metastatic colorectal cancer (IMblaze370): a multicentre, open-label, phase 3, randomised, controlled trial.** Lancet Oncol. 2019; 20:849-861. doi: 10.1016/S1470-2045(19)30027-0 (PMID: [31003911](#))
15. Lièvre A, et al. **KRAS mutations as an independent prognostic factor in patients with advanced colorectal cancer treated with cetuximab.** J Clin Oncol. 2008; 26:374-9. doi: 10.1200/JCO.2007.12.5906 (PMID: [18202412](#))
16. Janakiraman M, et al. **Genomic and biological characterization of exon 4 KRAS mutations in human cancer.** Cancer Res. 2010; 70:5901-11. doi: 10.1158/0008-5472.CAN-10-0192 (PMID: [20570890](#))
17. Stephen AG, et al. **Dragging ras back in the ring.** Cancer Cell. 2014; 25:272-81. doi: 10.1016/j.ccr.2014.02.017 (PMID: [24651010](#))
18. Pylayeva-Gupta Y, et al. **RAS oncogenes: weaving a tumorigenic web.** Nat Rev Cancer. 2011; 11:761-74. doi: 10.1038/nrc3106 (PMID: [21993244](#))
19. Zafra MP, et al. **An In Vivo Kras Allelic Series Reveals Distinct Phenotypes of Common Oncogenic Variants.** Cancer Discov. 2020; 10:1654-1671. doi: 10.1158/2159-8290.CD-20-0442 (PMID: [32792368](#))



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Name	Report No
-	26xxxxxxGR
20. Fisher GH, et al. Induction and apoptotic regression of lung adenocarcinomas by regulation of a K-Ras transgene in the presence and absence of tumor suppressor genes. Genes Dev. 2001; 15:3249-62. doi: 10.1101/gad.947701 (PMID: 11751631)	
21. Tidyman WE and Rauen KA. The RASopathies: developmental syndromes of Ras/MAPK pathway dysregulation. Curr Opin Genet Dev. 2009; 19:230-6. doi: 10.1016/j.gde.2009.04.001 (PMID: 19467855)	
22. Banerjee SN, et al. Efficacy and Safety of Avutemetinib ± Defactinib in Recurrent Low-Grade Serous Ovarian Cancer: Primary Analysis of ENGOT-OV60/GOG-3052/RAMP 201. J Clin Oncol. 2025; 43:2782-2792. doi: 10.1200/JCO-25-00112 (PMID: 40644648)	
23. Niihori T, et al. Germline KRAS and BRAF mutations in cardio-facio-cutaneous syndrome. Nat Genet. 2006; 38:294-6. doi: 10.1038/ng1749 (PMID: 16474404)	
24. Smith G, et al. Activating K-Ras mutations outwith 'hotspot' codons in sporadic colorectal tumours - implications for personalised cancer medicine. Br J Cancer. 2010; 102:693-703. doi: 10.1038/sj.bjc.6605534 (PMID: 20147967)	
25. AACR Project GENIE Consortium. AACR Project GENIE: Powering Precision Medicine through an International Consortium. Cancer Discov. 2017; 7:818-831. doi: 10.1158/2159-8290.CD-17-0151 (PMID: 28572459)	
26. Nusrat M and Yaeger R. KRAS inhibition in metastatic colorectal cancer: An update. Curr Opin Pharmacol. 2023; 68:102343. doi: 10.1016/j.coph.2022.102343 (PMID: 36638742)	
27. Higgs R. Screening: A re-evaluation of KRAS mutational 'hotspots'. Nat Rev Clin Oncol. 2010; 7:242. doi: 10.1038/nrclinonc.2010.54 (PMID: 20432530)	
28. Izeradjene K, et al. Kras(G12D) and Smad4/Dpc4 haploinsufficiency cooperate to induce mucinous cystic neoplasms and invasive adenocarcinoma of the pancreas. Cancer Cell. 2007; 11:229-43. doi: 10.1016/j.ccr.2007.01.017 (PMID: 17349581)	
29. Prior IA, et al. A comprehensive survey of Ras mutations in cancer. Cancer Res. 2012; 72:2457-67. doi: 10.1158/0008-5472.CAN-11-2612 (PMID: 22589270)	
30. Douillard JY, et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol. 2010; 28:4697-705. doi: 10.1200/JCO.2009.27.4860 (PMID: 20921465)	
31. Ahearn IM, et al. Regulating the regulator: post-translational modification of RAS. Nat Rev Mol Cell Biol. 2011; 13:39-51. doi: 10.1038/nrm3255 (PMID: 22189424)	
32. Tuveson DA, et al. Endogenous oncogenic K-ras(G12D) stimulates proliferation and widespread neoplastic and developmental defects. Cancer Cell. 2004; 5:375-87. doi: 10.1016/s1535-6108(04)00085-6 (PMID: 15093544)	
33. Douillard JY, et al. Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med. 2013; 369:1023-34. doi: 10.1056/NEJMoa1305275 (PMID: 24024839)	
34. Zenker M, et al. Expansion of the genotypic and phenotypic spectrum in patients with KRAS germline mutations. J Med Genet. 2007; 44:131-5. doi: 10.1136/jmg.2006.046300 (PMID: 17056636)	
35. Sabnis AJ, et al. Oncogenic Kras initiates leukemia in hematopoietic stem cells. PLoS Biol. 2009; 7:e59. doi: 10.1371/journal.pbio.1000059 (PMID: 19296721)	
36. Amado RG, et al. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol. 2008; 26:1626-34. doi: 10.1200/JCO.2007.14.7116 (PMID: 18316791)	
37. Caesar R, et al. Targeting MEK in vemurafenib-resistant hairy cell leukemia. Leukemia. 2019; 33:541-545. doi: 10.1038/s41375-018-0270-2 (PMID: 30341394)	



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