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Patient Name: 류재학
Gender: M
Sample ID: N25-326

Primary Tumor Site: Colon
Collection Date: 2025.11.26

Sample Cancer Type: Colon Cancer

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Relevant Colon Cancer Findings

Gene	Finding	Gene	Finding
BRAF	***BRAF p.(V600E) c.1799T>A***	NTRK3	None detected
ERBB2	None detected	PIK3CA	None detected
KRAS	None detected	POLD1	None detected
NRAS	None detected	POLE	None detected
NTRK1	None detected	RET	None detected
NTRK2	None detected		

Genomic Alteration	Finding
Microsatellite Status	***Microsatellite stable***
Tumor Mutational Burden	***3.78 Mut/Mb measured***

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

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*BRAF p.(V600E) c.1799T>A* B-Raf proto-oncogene, serine/threonine kinase Allele Frequency: 14.77% Locus: chr7:140453136 Transcript: NM_004333.6	**cetuximab + encorafenib** [1, 2 / I, II+] **cetuximab + encorafenib + chemotherapy** [1 / I, II+] **dabrafenib + trametinib** [1] encorafenib + panitumumab [I, II+] encorafenib + panitumumab + chemotherapy [I, II+] bevacizumab + chemotherapy [I]	**binimetinib + encorafenib** [1, 2 / I, II+] **cobimetinib + vemurafenib** [1, 2 / I, II+] **dabrafenib** [1, 2 / I, II+] **dabrafenib + trametinib** [1, 2 / I, II+] **vemurafenib** [1, 2 / I, II+] **atezolizumab + cobimetinib + vemurafenib** [1 / II+] **trametinib** [1, 2] cetuximab + encorafenib [I, II+] cetuximab + encorafenib + chemotherapy [I, II+] encorafenib [I, II+] encorafenib + panitumumab [I, II+]	38

*** Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], ESMO
*** Public data sources included in prognostic and diagnostic significance:** NCCN, ESMO
Line of therapy: I: First-line therapy, II+: Other line of therapy
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

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Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
			encorafenib + panitumumab + chemotherapy I, II+ ipilimumab + nivolumab I, II+ anti-PD-1 II+ dabrafenib + pembrolizumab + trametinib II+ ipilimumab II+ nivolumab II+ nivolumab + relatlimab II+ pembrolizumab II+ dabrafenib + MEK inhibitor selumetinib tovorafenib	
	Prognostic significance: ESMO: Poor			
IIC	*Microsatellite stable*	None*	None*	6
IIC	*PTPRK::RSPO3 fusion* protein tyrosine phosphatase receptor type K - R-spondin 3 Locus: chr6:128841404 - chr6:127469793	None*	None*	1
IIC	*RAD51 p.(M1?) c.1_2insA* RAD51 recombinase Allele Frequency: 44.91% Locus: chr15:40990955 Transcript: NM_133487.4	None*	None*	1

*** Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], ESMO
*** Public data sources included in prognostic and diagnostic significance:** NCCN, ESMO
Line of therapy: I: First-line therapy, II+: Other line of therapy
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

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

BRAF p.(V600E) c.1799T>A	**binimetinib + cetuximab + encorafenib** [1] **plixorafenib** [1]

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

Prevalent cancer biomarkers without relevant evidence based on included data sources

*BLM p.(L107Ffs*36) c.320_321insT, CIC p.(S1104T) c.3310T>A, RAD52 p.(S346*) c.1037C>A, SLX4 p.(A1221Cfs*67) c.3661_3662delGCinsT, TP53 p.(E294*) c.880G>T, UGT1A1 p.(G71R) c.211G>A, NQO1 p.(P187S) c.559C>T, SOX9 p.(Q340*) c.1018C>T, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
BRAF	p.(V600E)	c.1799T>A	COSM476	chr7:140453136	14.77%	NM_004333.6	missense
RAD51	p.(M1?)	c.1_2insA	.	chr15:40990955	44.91%	NM_133487.4	frameshift Insertion
BLM	p.(L107Ffs*36)	c.320_321insT	.	chr15:91292816	54.70%	NM_000057.4	frameshift Insertion

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Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
CIC	p.(S1104T)	c.3310T>A	.	chr19:42796852	47.15%	NM_015125.5	missense
RAD52	p.(S346*)	c.1037C>A	.	chr12:1023218	47.84%	NM_134424.4	nonsense
SLX4	p.(A1221Cfs*67)	c.3661_3662delGCinsT	.	chr16:3639977	32.52%	NM_032444.4	frameshift Block Substitution
TP53	p.(E294*)	c.880G>T	.	chr17:7577058	10.56%	NM_000546.6	nonsense
UGT1A1	p.(G71R)	c.211G>A	COSM4415616	chr2:234669144	50.30%	NM_000463.3	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	53.18%	NM_000903.3	missense
SOX9	p.(Q340*)	c.1018C>T	.	chr17:70120016	12.93%	NM_000346.4	nonsense
PIK3CB	p.(S53F)	c.158C>T	.	chr3:138478028	49.65%	NM_006219.3	missense
POM121L12	p.(V93F)	c.277G>T	.	chr7:53103641	49.42%	NM_182595.4	missense

Gene Fusions

Genes	Variant ID	Locus
PTPRK::RSPO3	PTPRK-RSPO3.P1R2.COSF1311.1	chr6:128841404 - chr6:127469793

Biomarker Descriptions

BRAF p.(V600E) c.1799T>A

B-Raf proto-oncogene, serine/threonine kinase

Background: The BRAF gene encodes the B-Raf proto-oncogene serine/threonine kinase, a member of the RAF family of serine/threonine protein kinases which also includes ARAF and RAF1(CRAF)[56]. BRAF is among the most commonly mutated kinases in cancer. Activation of the MAPK pathway occurs through BRAF mutations and leads to an increase in cell division, dedifferentiation, and survival[57,58]. BRAF mutations are categorized into three distinct functional classes, namely, class 1, 2, and 3, and are defined by the dependency on the RAS pathway[59]. Class 1 and 2 BRAF mutants are RAS-independent in that they signal as active monomers (Class 1) or dimers (Class 2) and become uncoupled from RAS GTPase signaling, resulting in constitutive activation of BRAF[59]. Class 3 mutants are RAS dependent as the kinase domain function is impaired or dead[59,60,61].

Alterations and prevalence: Somatic mutations in BRAF are observed in 59% of thyroid carcinoma, 53% of skin cutaneous melanoma, 12% of colorectal adenocarcinoma, 8% of lung adenocarcinoma, 5% of uterine corpus endometrial carcinoma, and 2-3% of bladder urothelial carcinoma, lung squamous cell carcinoma, stomach adenocarcinoma, cholangiocarcinoma, diffuse large B-cell lymphoma, glioblastoma multiforme, uterine carcinosarcoma, and head and neck squamous cell carcinoma[9,10]. Mutations at V600 belong to class 1 and include V600E, the most recurrent somatic BRAF mutation across diverse cancer types[60,62]. Class 2 mutations include K601E/N/T, L597Q/V, G469A/V/R, G464V/E, and BRAF fusions[60]. Class 3 mutations include D287H, V459L, G466V/E/A, S467L, G469E, and N581S/I[60]. BRAF V600E is universally present in hairy cell leukemia, mature B-cell cancers, and prevalent in histiocytic neoplasms[63,64,65]. Other recurrent BRAF somatic mutations cluster in the glycine-rich phosphate-binding loop at codons 464-469 in exon 11, as well as additional codons flanking V600 in the activation loop[62]. BRAF amplification is observed in 8% of ovarian serous cystadenocarcinoma, 4% of skin cutaneous melanoma, and 2% of sarcoma, uterine carcinosarcoma, and glioblastoma multiforme[9,10]. BRAF fusions are mutually exclusive to BRAF V600 mutations and have been described in melanoma, thyroid cancer, pilocytic astrocytoma, NSCLC, and several other cancer types[66,67,68,69,70]. Part of the oncogenic mechanism of BRAF gene fusions is the removal of the N-terminal auto-inhibitory domain, leading to constitutive kinase activation[61,66,68]. Alterations in BRAF are rare in pediatric cancers, with the most predominant being the V600E mutation and the BRAF::KIAA1549 fusion, both of which are observed in low-grade gliomas[71]. Somatic mutations are observed in 6% of glioma and less than 1% of bone cancer (2 in 327 cases), Wilms tumor (1 in 710 cases), and peripheral nervous system cancers (1 in 1158 cases)[9,10]. Amplification of BRAF is observed in 1% or less of Wilms tumor (2 in 136 cases) and B-lymphoblastic leukemia/lymphoma (2 in 731 cases)[9,10].

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Biomarker Descriptions (continued)

Potential relevance: Vemurafenib[72] (2011) is the first targeted therapy approved for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E mutation, and it is also approved for BRAF V600E-positive Erdheim-Chester Disease (2017). BRAF class 1 mutations, including V600E, are sensitive to vemurafenib, whereas class 2 and 3 mutations are insensitive[60]. BRAF kinase inhibitors including dabrafenib[73] (2013) and encorafenib[74] (2018) are also approved for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E/K mutations. Encorafenib[74] is approved in combination with cetuximab[75] (2020) for the treatment of BRAF V600E mutated colorectal cancer. Due to the tight coupling of RAF and MEK signaling, several MEK inhibitors have been approved for patients harboring BRAF alterations[60]. The MEK inhibitors, trametinib[76] (2013) and binimetinib[77] (2018), were approved for the treatment of metastatic melanoma with BRAF V600E/K mutations. Combination therapies of BRAF plus MEK inhibitors have been approved in melanoma and NSCLC[78]. The combinations of dabrafenib/trametinib[76](2015) and vemurafenib/cobimetinib[79] (2015) were approved for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E/K mutation. Subsequently, the combination of dabrafenib and trametinib was approved for metastatic NSCLC (2017), children with low-grade gliomas, and children and adults with solid tumors (2022) harboring a BRAF V600E mutation[73]. The PD-L1 antibody, atezolizumab[80], has also been approved in combination with cobimetinib and vemurafenib for BRAF V600 mutation-positive unresectable or metastatic melanoma. The FDA has granted fast track designation (2023) to ABM-1310[81] for BRAF V600E-mutated glioblastoma (GBM) patients. In 2018, binimetinib[82] was also granted breakthrough designation in combination with cetuximab and encorafenib for BRAF V600E mutant metastatic colorectal cancer. The ERK inhibitor ulixertinib[83] was granted fast track designation in 2020 for the treatment of patients with non-colorectal solid tumors harboring BRAF mutations G469A/V, L485W, or L597Q. The FDA granted fast track designation (2022) to the pan-RAF inhibitor, KIN-2787[84], for the treatment of BRAF class II or III alteration-positive malignant or unresectable melanoma. The FDA also granted fast track designation (2023) to the BRAF inhibitor, plixorafenib (PLX-8394)[85], for BRAF Class I (V600) and Class II (including fusions) altered cancer patients who have already undergone previous treatments. BRAF fusion is a suggested mechanism of resistance to BRAF targeted therapy in melanoma[86]. Additional mechanisms of resistance to BRAF targeted therapy include BRAF amplification, alternative splice transcripts, as well as activation of PI3K signaling and activating mutations in KRAS, NRAS, and MAP2K1/2 (MEK1/2)[87,88,89,90,91,92,93]. Clinical responses to sorafenib and trametinib in limited case studies of patients with BRAF fusions have been reported[70].

Microsatellite stable

Background: Microsatellites are short tandem repeats (STR) of 1 to 6 bases of DNA between 5 to 50 repeat units in length. There are approximately 0.5 million STRs that occupy 3% of the human genome[94]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[95,96]. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2[97]. Mutations and loss of expression in MMR genes, known as defective MMR (dMMR), lead to MSI. In contrast, when MMR genes lack alterations, they are referred to as MMR proficient (pMMR). Consensus criteria were first described in 1998 and defined MSI-high (MSI-H) as instability in two or more of the following five markers: BAT25, BAT26, D5S346, D2S123, and D17S250[98]. Tumors with instability in one of the five markers were defined as MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)[98]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[99,100,101,102,103]. MSI-H is a hallmark of Lynch syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes[96]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[95,96,100,104].

Alterations and prevalence: The MSI-H phenotype is observed in 30% of uterine corpus endothelial carcinoma, 20% of stomach adenocarcinoma, 15-20% of colon adenocarcinoma, and 5-10% of rectal adenocarcinoma[95,96,105,106]. MSI-H is also observed in 5% of adrenal cortical carcinoma and at lower frequencies in other cancers such as esophageal, liver, and ovarian cancers[105,106].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[107] (2014) and nivolumab[108] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[107] is also approved as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR with disease progression on prior therapy who are not candidates for surgery or radiation. Importantly, pembrolizumab is approved for the treatment of MSI-H or dMMR solid tumors that have progressed following treatment, with no alternative option and is the first anti-PD-1 inhibitor to be approved with a tumor agnostic indication[107]. Dostarlimab[109] (2021) is also approved for dMMR recurrent or advanced endometrial carcinoma or solid tumors that have progressed on prior treatment and is recommended as a subsequent therapy option in dMMR/MSI-H advanced or metastatic colon or rectal cancer[101,110]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[111] (2011), is approved alone or in combination with nivolumab in MSI-H or dMMR colorectal cancer that has progressed following treatment with chemotherapy. MSI-H may confer a favorable prognosis in colorectal cancer although outcomes vary depending on stage and tumor location[101,112,113]. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients[113]. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H tumors[114,115]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[114,115].

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Biomarker Descriptions (continued)

PTPRK::RSPO3 fusion

R-spondin 3, protein tyrosine phosphatase receptor type K

Background: The RSPO3 gene encodes R-spondin 3 protein, a member of the R-spondin family of secreted protein ligands, which includes RSPO1, RSPO2, and RSPO4[1,2]. R-spondin proteins contribute to the regulation of the Wnt signaling pathway, the activation of which can lead to the expression of genes that control cell proliferation, migration, and cell polarity formation[2,3,4]. Specifically, Wnt signaling receptors LGR4, LGR5, and LGR6 have been shown to bind to RSPO2 and RSPO3 to enhance Wnt/beta-catenin signaling[5,6]. Aberrations in the Wnt signaling pathway, including RSPO3 rearrangement, have been observed to lead to Wnt activation, thereby influencing cancer development and progression[7,8].

Alterations and prevalence: Rearrangements of RSPO3 that lead to protein fusions are observed to potentiate Wnt signalling and have been identified to be recurrent in colon cancer[8]. In one study, the RSPO3::PTPRK fusion was identified in 5/68 (8%) of colon tumor samples[8]. RSPO3 fusions are also observed in 1% of sarcoma[9,10]. Somatic RSPO3 mutations are observed in 3% of uterine corpus endometrial carcinoma, 2% of skin cutaneous melanoma, and colorectal adenocarcinoma[9,10].

Potential relevance: Currently, no therapies are approved for RSPO3 aberrations.

RAD51 p.(M1?) c.1_2insA

RAD51 recombinase

Background: The RAD51 gene encodes the RAD51 recombinase protein and is a member of the RAD51 protein family that also includes RAD51B (RAD51L1), RAD51C (RAD51L2), RAD51D (RAD51L3), XRCC2, and XRCC3 paralogs. The RAD51 family proteins are involved in homologous recombination repair (HRR) and DNA repair of double-strand breaks (DSB)[23]. RAD51 interacts with many DNA repair and cell cycle genes, including BRCA1, BRCA2, p53, and ATM[24]. RAD51 is expressed in proliferating cells in the S or S/G2 phases of the cell cycle and mediates DNA strand invasion and homologous pairing between DNA duplexes[25,26]. RAD51 is a tumor suppressor gene. Loss of function mutations in RAD51 can lead to deficiencies in DSB repair and are implicated in the BRCAness phenotype, which is characterized by a defect in HRR, mimicking BRCA1 or BRCA2 loss[25,27,28].

Alterations and prevalence: Somatic mutations in RAD51 have been described in breast and prostate cancers[24].

Potential relevance: Currently, no therapies are approved for RAD51 aberrations.

BLM p.(L107Ffs*36) c.320_321insT

Bloom syndrome RecQ like helicase

Background: The BLM gene encodes the BLM RecQ like helicase, a protein responsible for the unwinding of various DNA substrates[1]. During homologous recombination repair (HRR), BLM forms a complex with TOP3A, RMI1, and RMI2, which facilitates the separation of repaired/template DNA and Holliday junction resolution[14,15]. BLM also functions as an endonuclease in end resection during HRR and is capable of displacing RAD51 from DNA strand breaks, thereby preventing further recombination in the end stages of HRR[14,16]. Germline BLM mutations result in Bloom Syndrome, a recessive genetic disorder that is classified by chromosomal breakage and causes a predisposition for gastrointestinal cancer, bladder cancer, skin cancer, B-cell and T-cell immunodeficiencies[17].

Alterations and prevalence: Somatic mutations in BLM are observed in 7% of uterine corpus endometrial carcinoma, 4% of bladder urothelial carcinoma and colorectal adenocarcinoma, 3% of stomach adenocarcinoma, skin cutaneous melanoma, and cholangiocarcinoma[9,10].

Potential relevance: Currently, no therapies are approved for BLM aberrations. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[18], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers.

CIC p.(S1104T) c.3310T>A

capicua transcriptional repressor

Background: The CIC gene encodes the capicua transcriptional repressor, a member of the high mobility group (HMG)-box superfamily[1,19]. The HMG-box domain mediates CIC binding to an octameric consensus sequence at the promoters of target genes[1,19]. CIC interacts with the HDAC complex and SWI/SNF to transcriptionally repress target genes, which include members of the E-Twenty Six (ETS) oncogene family ETV1, ETV4 and ETV5[19]. CIC aberrations lead to increased RTK/MAPK signaling and oncogenesis, supporting a tumor suppressor role for CIC[19].

Biomarker Descriptions (continued)

Alterations and prevalence: Somatic mutations in CIC are observed in 21% of brain lower grade glioma, 11% of uterine corpus endometrial carcinoma, 8% of skin cutaneous melanoma, 7% of stomach adenocarcinoma, and 6% of colorectal adenocarcinoma[9,10]. Biallelic loss of CIC is observed 2% of prostate adenocarcinoma and diffuse large B-cell lymphoma (DLBCL)[9,10]. Recurrent CIC fusions are found in Ewing-like sarcoma (ELS) (CIC::DUX4 and CIC::FOXO4), angiosarcoma (CIC::LEUTX), peripheral neuroectodermal tumors (CIC::NUTM1) and oligodendroglioma[19,20].

Potential relevance: Currently, no therapies are approved for CIC aberrations. CIC fusions, including CIC::DUX4 fusion, t(10;19)(q26;q13) and t(4;19)(q35;q13), are ancillary diagnostic markers for CIC-Rearranged Sarcoma[21,22].

RAD52 p.(S346*) c.1037C>A

RAD52 homolog, DNA repair protein

Background: The RAD52 gene encodes the RAD52 homolog, DNA repair protein[1]. RAD52 binds to single- and double-stranded DNA and enables strand exchange for double-strand break (DSB) repair by binding to RAD51[29]. RAD52 also promotes DSB repair through homologous recombination repair (HRR) by recruiting BRCA1 to sites of DSBs, which leads to the removal of TP53BP1 and prevents DSB repair by non-homologous end joining (NHEJ)[30].

Alterations and prevalence: Somatic mutations in RAD52 are observed in 2% of uterine corpus endometrial carcinoma, uterine carcinosarcoma, and skin cutaneous melanoma[9,10].

Potential relevance: Currently, no therapies are approved for RAD52 aberrations.

SLX4 p.(A1221Cfs*67) c.3661_3662delGCinsT

SLX4 structure-specific endonuclease subunit

Background: The SLX4 gene encodes the SLX4 structure-specific endonuclease subunit[1]. SLX4, also known as FANCP, is a tumor suppressor protein that functions as a scaffold for DNA repair endonucleases[11]. SLX4 functions in DNA repair mechanisms including double-strand break (DSB) repair and interstrand crosslink repair[11,12,13]. Specifically, SLX4 localizes at DSB sites and recruits and interacts with other repair proteins such as ERCC1-XPF, MUS81-EME1, and SLX1[11,12,13]. Germline SLX4 mutations are associated with Fanconi Anemia, a genetic condition characterized by genomic instability and congenital abnormalities, including bone marrow failure and cancer predisposition[12].

Alterations and prevalence: Recurrent somatic mutations in SLX4 are observed in 11% of uterine corpus endometrial carcinoma, 9% of skin cutaneous melanoma, 6% of stomach adenocarcinoma, and 4% of bladder urothelial carcinoma[9,10].

Potential relevance: Currently, no therapies are approved for SLX4 aberrations.

TP53 p.(E294*) c.880G>T

tumor protein p53

Background: The TP53 gene encodes the tumor suppressor protein p53, which binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair[1]. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis[31]. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential[32]. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[33,34].

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)[9,10,35,36,37,38]. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common, including substitutions at codons R158, R175, Y220, R248, R273, and R282[9,10]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[39,40,41,42]. Alterations in TP53 are also observed in pediatric cancers[9,10]. Somatic mutations are observed in 53% of non-Hodgkin lymphoma, 24% of soft tissue sarcoma, 19% of glioma, 13% of bone cancer, 9% of B-lymphoblastic leukemia/lymphoma, 4% of embryonal tumors, 3% of Wilms tumor and leukemia, 2% of T-lymphoblastic leukemia/lymphoma, and less than 1% of peripheral nervous system cancers (5 in 1158 cases)[9,10]. Biallelic loss of TP53 is observed in 10% of bone cancer, 2% of Wilms tumor, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and leukemia (1 in 250 cases)[9,10].

Potential relevance: The small molecule p53 reactivator, PC14586[43] (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. In addition to investigational therapies aimed at restoring wild-type TP53

Biomarker Descriptions (continued)

activity, compounds that induce synthetic lethality are also under clinical evaluation[44,45]. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma[46]. TP53 mutations confer poor prognosis and poor risk in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)[47,48,49,50,51]. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[52]. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occurring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system[53].

UGT1A1 p.(G71R) c.211G>A

UDP glucuronosyltransferase family 1 member A1

Background: The UGT1A1 gene encodes UDP glucuronosyltransferase family 1 member A1, a member of the UDP-glucuronosyltransferase 1A (UGT1A) subfamily of the UGT protein superfamily[1,116]. UGTs are microsomal membrane-bound enzymes that catalyze the glucuronidation of endogenous and xenobiotic compounds and transform the lipophilic molecules into excretable, hydrophilic metabolites[116,117]. UGTs play an important role in drug metabolism, detoxification, and metabolite homeostasis. Differential expression of UGTs can promote cancer development, disease progression, as well as drug resistance[118]. Specifically, elevated expression of UGT1As are associated with resistance to many anti-cancer drugs due to drug inactivation and lower active drug concentrations. However, reduced expression and downregulation of UGT1As are implicated in bladder and hepatocellular tumorigenesis and progression due to toxin accumulation[118,119,120,121]. Furthermore, UGT1A1 polymorphisms, such as UGT1A1*28, UGT1A1*93, and UGT1A1*6, confer an increased risk of severe toxicity to irinotecan-based chemotherapy treatment of solid tumors, due to reduced glucuronidation of the irinotecan metabolite, SN-38[122].

Alterations and prevalence: Biallelic deletion of UGT1A1 has been observed in 6% of sarcoma, 3% of brain lower grade glioma and uveal melanoma, and 2% of thymoma, cervical squamous cell carcinoma, bladder urothelial carcinoma, head and neck squamous cell carcinoma, and esophageal adenocarcinoma[9,10].

Potential relevance: Currently, no therapies are approved for UGT1A1 aberrations.

SOX9 p.(Q340*) c.1018C>T

SRY-box 9

Background: The SOX9 gene encodes the SRY-box transcription factor 9 protein[1]. SOX9 regulates developmental pathways including stemness, differentiation, and progenitor development[54]. SOX9 has been shown to regulate cell cycle progression and cell proliferation[54]. In cancer, SOX9 aberrations have been observed to confer both gain or loss of function depending on the cancer type, supporting both tumor suppressor and oncogenic roles for SOX9[55].

Alterations and prevalence: Somatic mutations in SOX9 are predominantly missense or truncating and are observed in 12% of colorectal adenocarcinoma, 4% of uterine corpus endometrial carcinoma, and 3% of stomach adenocarcinoma[9,10]. Amplification of SOX9 is observed in 3% of sarcoma, breast invasive carcinoma, mesothelioma, esophageal adenocarcinoma, and liver hepatocellular carcinoma, 2% of stomach adenocarcinoma, bladder urothelial carcinoma, lung adenocarcinoma, skin cutaneous melanoma, lung squamous cell carcinoma, uterine carcinosarcoma, brain lower grade glioma, pancreatic adenocarcinoma, thymoma, and ovarian serous cystadenocarcinoma, and 1% of cervical squamous cell carcinoma, pheochromocytoma and paraganglioma, uterine corpus endometrial carcinoma and prostate adenocarcinoma[9,10]. Biallelic deletion is also observed in 1% of uveal melanoma, sarcoma, and stomach adenocarcinoma[9,10].

Potential relevance: Currently, no therapies are approved for SOX9 aberrations.

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Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2025-09-17. For the most up-to-date information, search www.fda.gov.

BRAF p.(V600E) c.1799T>A

binimetinib + cetuximab + encorafenib

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Supporting Statement:
The FDA has granted Breakthrough Therapy designation to the MEK inhibitor, binimetinib, in combination with cetuximab and encorafenib for BRAF V600E mutant metastatic colorectal cancer.

Reference:

https://markets.businessinsider.com/news/stocks/array-biopharma-receives-fda-breakthrough-therapy-designation-for-braftovi-in-combination-with-mektovi-and-cetuximab-for-brafv600e-mutant-metastatic-colorectal-cancer-1027437791

plixorafenib

Cancer type: Solid Tumor

Variant class: BRAF V600 mutation

Supporting Statement:
The FDA has granted Fast Track designation to a novel small molecule inhibitor, plixorafenib (PLX-8394), for the treatment of patients with cancers harboring BRAF Class 1 (V600) and Class 2 (including fusions) alterations who have exhausted prior therapies.

Reference:

https://fore.bio/fore-biotherapeutics-announces-fast-track-designation-granted-by-fda-to-fore8394-for-the-treatment-of-cancers-harboring-braf-class-1-and-class-2-alterations/

ABM-1310

Cancer type: Glioblastoma IDH-wildtype (Grade 4)

Variant class: BRAF V600E mutation

Supporting Statement:
The FDA has granted Fast Track designation to ABM-1310 for the treatment of glioblastoma (GBM) patients with BRAF V600E mutation.

Reference:

https://www.prnewswire.com/news-releases/abm-therapeutics-abm-1310-granted-fast-track-designation-by-the-fda-following-orphan-drug-designation-301937168.html

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4,

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Genes Assayed (continued)

Genes Assayed for the Detection of DNA Sequence Variants (continued)

IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLCO1B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XPO1, ZNF217, ZNF429

Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4, ERRFI1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, FGF4, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FUBP1, FYN, GATA2, GATA3, GLI3, GNA13, GNAS, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, IDH2, IGF1R, IKBKB, IL7R, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LARP4B, LATS1, LATS2, MAGOH, MAP2K1, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK1, MAPK8, MAX, MCL1, MDM2, MDM4, MECOM, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLH3, MPL, MRE11, MSH2, MSH3, MSH6, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLCO1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSPO2, RSPO3, TERT

Genes Assayed with Full Exon Coverage

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBFB, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRFI1, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXW7, FUBP1, GATA3, GNA13, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, ID3, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KEAP1, KLHL13, KMT2A, KMT2B, KMT2C, KMT2D, LARP4B, LATS1, LATS2, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK8, MEN1, MGA, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MTAP, MTUS2, MUTYH, NBN, NCOR1, NF1, NF2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PDCD1, PDCD1LG2, PDIA3, PGD, PHF6, PIK3R1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R2A, PRDM1, PRDM9, PRKAR1A, PSMB10, PSMB8, PSMB9, PTCH1, PTEN, PTPRT, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RASA1, RASA2, RB1, RBM10, RECQL4, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPA1, RPL22, RPL5, RUNX1, RUNX1T1, SDHA, SDHB, SDHC, SDHD, SETD2, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SOCS1, SOX9, SPEN, STAG2, STAT1, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TET2, TGFBR2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFHX3, ZMYM3, ZRSR2

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Relevant Therapy Summary

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

BRAF p.(V600E) c.1799T>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
dabrafenib + trametinib	◑	○	○	○	✖
cetuximab + encorafenib	●	◑	●	●	✖
cetuximab + encorafenib + FOLFOX	●	◑	✖	✖	✖
cobimetinib + vemurafenib	○	○	○	○	● (II/III)
binimetinib + encorafenib	○	○	○	○	✖
dabrafenib	○	○	○	✖	● (II)
trametinib	○	○	○	✖	✖
vemurafenib	○	○	○	✖	✖
atezolizumab + cobimetinib + vemurafenib	○	○	✖	✖	✖
encorafenib + panitumumab	✖	◑	✖	✖	✖
encorafenib + panitumumab + FOLFOX	✖	◑	✖	✖	✖
encorafenib	✖	○	✖	○	✖
dabrafenib + pembrolizumab + trametinib	✖	○	✖	✖	✖
selumetinib	✖	○	✖	✖	✖
tovorafenib	✖	○	✖	✖	✖
bevacizumab + CAPOX	✖	✖	✖	●	✖
bevacizumab + FOLFOX	✖	✖	✖	●	✖
bevacizumab + FOLFOXIRI	✖	✖	✖	●	✖
anti-PD-1	✖	✖	✖	○	✖
dabrafenib + MEK inhibitor	✖	✖	✖	○	✖
ipilimumab	✖	✖	✖	○	✖
ipilimumab + nivolumab	✖	✖	✖	○	✖
nivolumab	✖	✖	✖	○	✖
nivolumab + relatlimab	✖	✖	✖	○	✖
pembrolizumab	✖	✖	✖	○	✖
encorafenib, binimetinib, cetuximab	✖	✖	✖	✖	● (III)
cetuximab, binimetinib, encorafenib	✖	✖	✖	✖	● (II/III)
bevacizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, chemotherapy, leucovorin	✖	✖	✖	✖	● (II)

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

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Relevant Therapy Summary (continued)

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

BRAF p.(V600E) c.1799T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
camrelizumab, regorafenib, fruquintinib	✖	✖	✖	✖	● (II)
cetuximab, encorafenib	✖	✖	✖	✖	● (II)
cetuximab, encorafenib, binimetinib	✖	✖	✖	✖	● (II)
cetuximab, panitumumab, encorafenib, antimalarial	✖	✖	✖	✖	● (II)
cetuximab, vemurafenib, chemotherapy	✖	✖	✖	✖	● (II)
chemotherapy, cetuximab, dabrafenib, panitumumab	✖	✖	✖	✖	● (II)
encorafenib, cetuximab, bevacizumab	✖	✖	✖	✖	● (II)
encorafenib, cetuximab, chemotherapy	✖	✖	✖	✖	● (II)
KN046, regorafenib	✖	✖	✖	✖	● (II)
plixorafenib, cobicistat	✖	✖	✖	✖	● (II)
tunlametinib, vemurafenib	✖	✖	✖	✖	● (II)
vemurafenib, cetuximab, chemotherapy	✖	✖	✖	✖	● (II)
vemurafenib, cetuximab, chemotherapy, bevacizumab	✖	✖	✖	✖	● (II)
chemotherapy, KSQ-004, aldesleukin	✖	✖	✖	✖	● (I/II)
donafenib, trametinib, cetuximab, chemotherapy	✖	✖	✖	✖	● (I/II)
RX208, serplulimab	✖	✖	✖	✖	● (I/II)
RX208, trametinib	✖	✖	✖	✖	● (I/II)
BDTX-4933	✖	✖	✖	✖	● (I)
CGX-1321, encorafenib, cetuximab	✖	✖	✖	✖	● (I)
daraxonrasib	✖	✖	✖	✖	● (I)
exarafenib, binimetinib	✖	✖	✖	✖	● (I)
HSK42360	✖	✖	✖	✖	● (I)
JSI-1187	✖	✖	✖	✖	● (I)
PF-07799933, cetuximab, binimetinib	✖	✖	✖	✖	● (I)
RO-7276389, cobimetinib	✖	✖	✖	✖	● (I)
RX208	✖	✖	✖	✖	● (I)
ulixertinib, cetuximab, encorafenib	✖	✖	✖	✖	● (I)
ZEN-3694, binimetinib	✖	✖	✖	✖	● (I)
ZEN-3694, cetuximab, encorafenib	✖	✖	✖	✖	● (I)

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

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Relevant Therapy Summary (continued)

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

Microsatellite stable

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
encorafenib, binimetinib, cetuximab	✖	✖	✖	✖	● (III)
camrelizumab, regorafenib, fruquintinib	✖	✖	✖	✖	● (II)
cetuximab, encorafenib, binimetinib	✖	✖	✖	✖	● (II)
chemotherapy, cetuximab, dabrafenib, panitumumab	✖	✖	✖	✖	● (II)
encorafenib, cetuximab, bevacizumab	✖	✖	✖	✖	● (II)
KN046, regorafenib	✖	✖	✖	✖	● (II)

PTPRK::RSPO3 fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
CGX-1321, encorafenib, cetuximab	✖	✖	✖	✖	● (I)

RAD51 p.(M1?) c.1_2insA

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
talazoparib	✖	✖	✖	✖	● (II)

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

HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	***0.0%***
Not Detected	***Not Applicable***

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L.

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.10(006)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-09-17. NCCN information was sourced from www.nccn.org and is current as of 2025-09-02. EMA information was sourced from www.ema.europa.eu and is current as of 2025-09-17. ESMO information was sourced from www.esmo.org and is current as of 2025-09-02. Clinical Trials information is current as of 2025-09-02. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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