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Patient Name: 박재범
Gender: Male
Sample ID: N26-23

Primary Tumor Site: Pancreas
Collection Date: 2026.01.12.

Sample Cancer Type: Pancreatic Cancer

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Relevant Pancreatic Cancer Findings

Gene	Finding	Gene	Finding
BRAF	None detected	KRAS	None detected
BRCA1	None detected	NRG1	None detected
BRCA2	None detected	NTRK1	None detected
ERBB2	None detected	NTRK2	None detected
FGFR1	None detected	NTRK3	***NTRK3 amplification***
FGFR2	None detected	PALB2	None detected
FGFR3	None detected	RET	None detected

Genomic Alteration	Finding
Tumor Mutational Burden	***15.15 Mut/Mb measured***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*MTAP deletion* methylthioadenosine phosphorylase Locus: chr9:21802646	None*	None*	15
IIC	*CDKN2A deletion* cyclin dependent kinase inhibitor 2A Locus: chr9:21968178	None*	None*	5
IIC	*CCND1 amplification* cyclin D1 Locus: chr11:69455949	None*	None*	2
IIC	*CDKN2B deletion* cyclin dependent kinase inhibitor 2B Locus: chr9:22005728	None*	None*	2

*** 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
IIC	*NTRK3 amplification* neurotrophic receptor tyrosine kinase 3 Locus: chr15:88420191	None*	None*	2
IIC	*FGF19 amplification* fibroblast growth factor 19 Locus: chr11:69513948	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.

Prevalent cancer biomarkers without relevant evidence based on included data sources

ASXL2 p.(R312) c.934C>T, FGF3 amplification, FGF4 amplification, MSH3 p.(A57Pfs*14) c.162_196delTGCAGCGGCCGCAGCGGCCGCAGCGCCCCCAGCGCinsCGCAGCG, Microsatellite stable, NFE2L2 p.(W24C) c.72G>C, TP53 p.(V157F) c.469G>T, FMO3 p.(S310L) c.929C>T, HLA-B deletion, IDH2 amplification, IGF1R amplification, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ASXL2	p.(R312*)	c.934C>T	.	chr2:25982356	36.82%	NM_018263.6	nonsense
MSH3	p.(A57Pfs*14)	c.162_196delTGCAGCGGCCGCAGCGGCCGCAGCGCCCCCAGCGCinsCGCAGCG	.	chr5:79950708	1.67%	NM_002439.5	frameshift Block Substitution
NFE2L2	p.(W24C)	c.72G>C	COSM132852	chr2:178098973	21.34%	NM_006164.5	missense
TP53	p.(V157F)	c.469G>T	COSM10670	chr17:7578461	38.69%	NM_000546.6	missense
FMO3	p.(S310L)	c.929C>T	.	chr1:171083248	23.64%	NM_006894.6	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	28.63%	NM_000903.3	missense
SPEN	p.(K1452N)	c.4356A>T	.	chr1:16257091	15.20%	NM_015001.3	missense
REG1A	p.(E52Q)	c.154G>C	.	chr2:79348777	10.66%	NM_002909.5	missense
CNTN6	p.(L811V)	c.2431C>G	.	chr3:1425006	14.81%	NM_014461.4	missense
P2RY1	p.(L244F)	c.732G>C	.	chr3:152554303	4.55%	NM_002563.5	missense
MSH3	p.(A57_A62del)	c.162_179delTGCAGCGGCCGCAGCGGC	.	chr5:79950707	96.75%	NM_002439.5	nonframeshift Deletion
HLA-B	p.([T118I;L119I])	c.353_355delCCCinsTCA	.	chr6:31324208	96.00%	NM_005514.8	missense, missense
NOTCH4	p.(D606H)	c.1816G>C	.	chr6:32184767	39.31%	NM_004557.4	missense
HDAC9	p.(L413I)	c.1237C>A	.	chr7:18687609	11.57%	NM_178425.3	missense
HDAC9	p.(K816N)	c.2448G>C	.	chr7:18869153	4.45%	NM_178425.3	missense
GLI3	p.(R990C)	c.2968C>T	.	chr7:42005703	12.76%	NM_000168.6	missense

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Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
CSMD3	p.(?)	c.4896-4_4896-3delinsGT	.	chr8:113516209	4.00%	NM_198123.2	unknown
PCDH15	p.(G18S)	c.52G>A	.	chr10:56423971	16.21%	NM_001142763.2	missense
STAT6	p.(R115C)	c.343C>T	.	chr12:57500611	10.15%	NM_003153.5	missense
CAMKK2	p.(T362S)	c.1084A>T	.	chr12:121691099	46.29%	NM_001270485.2	missense
BLM	p.(R898K)	c.2693G>A	.	chr15:91328181	31.36%	NM_000057.4	missense
PPM1D	p.(T529N)	c.1586C>A	.	chr17:58740681	13.08%	NM_003620.4	missense
BRIP1	p.(S1031C)	c.3092C>G	.	chr17:59761315	11.86%	NM_032043.3	missense
MAP2K7	p.(?)	c.567+3G>A	.	chr19:7975460	3.25%	NM_145185.4	unknown
KEAP1	p.(R596Q)	c.1787G>A	.	chr19:10597416	13.41%	NM_203500.2	missense
CST5	p.(S53C)	c.157A>T	.	chr20:23860157	14.53%	NM_001900.5	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
MTAP	chr9:21802646	0.35	0.67
CDKN2A	chr9:21968178	0.15	0.63
CCND1	chr11:69455949	28.48	6.29
CDKN2B	chr9:22005728	0.15	0.63
NTRK3	chr15:88420191	4.93	1.59
FGF19	chr11:69513948	30.3	6.66
FGF3	chr11:69625020	11.38	2.88
FGF4	chr11:69588019	9.25	2.45
HLA-B	chr6:31322252	0	0.43
IDH2	chr15:90628015	5.48	1.7
IGF1R	chr15:99192814	5.33	1.67
FANCF	chr11:22646196	4.88	1.57
FANCI	chr15:89790860	5.45	1.69
BLM	chr15:91290599	5.15	1.63

Biomarker Descriptions

MTAP deletion

methylthioadenosine phosphorylase

Background: The MTAP gene encodes methylthioadenosine phosphorylase[1]. Methylthioadenosine phosphorylase, a key enzyme in polyamine biosynthesis and methionine salvage pathways, catalyzes the reversible phosphorylation of S-methyl-5'-thioadenosine (MTA) to adenine and 5-methylthioribose-1-phosphate[7,8]. Loss of MTAP function is commonly observed in cancer due to deletion or

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Biomarker Descriptions (continued)

promotor methylation which results in the loss of MTA phosphorylation and sensitivity of MTAP-deficient cells to purine synthesis inhibitors and to methionine deprivation[8].

Alterations and prevalence: MTAP is flanked by CDKN2A tumor suppressor on chromosome 9p21 and is frequently found to be co-deleted with CDKN2A in numerous solid and hematological cancers[8,9]. Consequently, biallelic loss of MTAP has been observed in 42% of glioblastoma multiforme, 32% of mesothelioma, 26% of bladder urothelial carcinoma, 22% of pancreatic adenocarcinoma, 21% of esophageal adenocarcinoma, 20% of lung squamous cell carcinoma and skin cutaneous melanoma, 15% of diffuse large B-cell lymphoma and head and neck squamous cell carcinoma, 12% of lung adenocarcinoma, 11% of cholangiocarcinoma, 9% of sarcoma, stomach adenocarcinoma and brain lower grade glioma, and 3% of ovarian serous cystadenocarcinoma, breast invasive carcinoma, adrenocortical carcinoma, thymoma and liver hepatocellular carcinoma[5,6]. Somatic mutations in MTAP have been found in 3% of uterine corpus endometrial carcinoma[5,6].

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

CDKN2A deletion

cyclin dependent kinase inhibitor 2A

Background: CDKN2A encodes cyclin dependent kinase inhibitor 2A, a cell cycle regulator that controls G1/S progression[1]. CDKN2A, also known as p16/INK4A, belongs to a family of INK4 cyclin-dependent kinase inhibitors, which also includes CDKN2B (p15/INK4B), CDKN2C (p18/INK4C), and CDKN2D (p19/INK4D)[10]. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb[11,12,13]. CDKN2A encodes two alternative transcript variants, namely p16 and p14ARF, both of which exhibit differential tumor suppressor functions[14]. Specifically, the CDKN2A/p16 transcript inhibits cell cycle kinases CDK4 and CDK6, whereas the CDKN2A/p14ARF transcript stabilizes the tumor suppressor protein p53 to prevent its degradation[1,14,15]. CDKN2A aberrations commonly co-occur with CDKN2B[10]. Loss of CDKN2A/p16 results in downstream inactivation of the Rb and p53 pathways, leading to uncontrolled cell proliferation[16]. Germline mutations of CDKN2A are known to confer a predisposition to melanoma and pancreatic cancer[17,18].

Alterations and prevalence: Somatic alterations in CDKN2A often result in loss of function (LOF) which is attributed to copy number loss, truncating, or missense mutations[19]. Somatic mutations in CDKN2A are observed in 20% of head and neck squamous cell carcinoma and pancreatic adenocarcinoma, 15% of lung squamous cell carcinoma, 13% of skin cutaneous melanoma, 8% of esophageal adenocarcinoma, 7% of bladder urothelial carcinoma, 6% of cholangiocarcinoma, 4% of lung adenocarcinoma and stomach adenocarcinoma, and 2% of liver hepatocellular carcinoma, uterine carcinosarcoma, and cervical squamous cell carcinoma[5,6]. Biallelic deletion of CDKN2A is observed in 56% of glioblastoma multiforme, 45% of mesothelioma, 39% of esophageal adenocarcinoma, 32% of bladder urothelial carcinoma, 31% of skin cutaneous melanoma and head and neck squamous cell carcinoma, 28% of pancreatic adenocarcinoma, 27% of diffuse large B-cell lymphoma, 26% of lung squamous cell carcinoma, 17% of lung adenocarcinoma and cholangiocarcinoma, 15% of sarcoma, 11% of stomach adenocarcinoma and of brain lower grade glioma, 7% of adrenocortical carcinoma, 6% of liver hepatocellular carcinoma, 4% of breast invasive carcinoma, kidney renal papillary cell carcinoma and thymoma, 3% of ovarian serous cystadenocarcinoma and kidney renal clear cell carcinoma, and 2% of uterine carcinosarcoma and kidney chromophobe[5,6]. Alterations in CDKN2A are also observed in pediatric cancers[6]. Biallelic deletion of CDKN2A is observed in 68% of T-lymphoblastic leukemia/lymphoma, 40% of B-lymphoblastic leukemia/lymphoma, 25% of glioma, 19% of bone cancer, and 6% of embryonal tumors[6]. Somatic mutations in CDKN2A are observed in less that 1.5% of bone cancer (5 in 327 cases), B-lymphoblastic leukemia/lymphoma (3 in 252 cases), and leukemia (1 in 354 cases)[6].

Potential relevance: Loss of CDKN2A can be useful in the diagnosis of mesothelioma, and mutations in CDKN2A are ancillary diagnostic markers of malignant peripheral nerve sheath tumors[20,21,22]. Additionally, deletion of CDKN2B is a molecular marker used in staging Grade 4 pediatric IDH-mutant astrocytoma[23]. Currently, no therapies are approved for CDKN2A aberrations. However, CDKN2A LOF leading to CDK4/6 activation may confer sensitivity to CDK inhibitors such as palbociclib and abemaciclib[24,25,26]. Alternatively, CDKN2A expression and Rb inactivation demonstrate resistance to palbociclib in cases of glioblastoma multiforme[27]. CDKN2A (p16) expression is associated with a favorable prognosis for progression-free survival (PFS) and overall survival (OS) in p16/HPV positive head and neck cancer[28,29,30,31].

CCND1 amplification

cyclin D1

Background: The CCND1 gene encodes the cyclin D1 protein, a member of the highly conserved D-cyclin family that also includes CCND2 and CCND3[145,146,147]. D-type cyclins are known to regulate cell cycle progression by binding to and activating cyclin dependent kinases (CDKs), specifically CDK4 and CDK6, which leads to the phosphorylation and inactivation of the retinoblastoma (RB1) protein[145,146]. Consequently, RB1 inactivation results in E2F transcription factor activation and cellular G1/S phase transition thereby resulting in cell cycle progression, a common event observed in tumorigenesis[145,146,148]. Aberrations in the D-type cyclins have been observed to promote tumor progression suggesting an oncogenic role for CCND1[147,149].

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Biomarker Descriptions (continued)

Alterations and prevalence: Recurrent somatic alterations to CCND1, including mutations, amplifications, and chromosomal translocations, are observed in many cancer types. A common mechanism of these alterations is to increase the expression and nuclear localization of the cyclin D1 protein. Recurrent somatic mutations include missense mutations at codons T286 and P287 and c-terminal truncating mutations that are enriched in about 33% of uterine cancer, and missense mutations at Y44 that are enriched in about 50% of Mantle cell lymphoma (MCL)[5,6,150,151]. These mutations block phosphorylation-dependent nuclear export and proteolysis[152,153,154,155]. CCND1 is recurrently amplified in many cancer types, including up to 35% of esophageal cancer, 20-30% of head and neck cancer, and 10-20% of breast, squamous lung, and bladder cancers[5,6,56]. MCL is genetically characterized by the t(11;14)(q13;q13) translocation, a rearrangement that juxtaposes CCND1 to the immunoglobulin heavy (IgH) chain gene. This rearrangement leads to constitutive expression of cyclin D1 and plays an important role in MCL pathogenesis[156,157]. Alterations in CCND1 are also observed in pediatric cancers[6]. Amplification of CCND1 is observed in 1-3% of peripheral nervous system tumors (3 in 91 cases) and bone cancer (1 in 42 cases) and less than 1% of Wilms tumor (1 in 136 cases) and B-lymphoblastic leukemia/lymphoma (2 in 731 cases)[6].

Potential relevance: Currently, no therapies are approved for CCND1 aberrations. The t(11;14) translocation involving CCND1 can be used to help diagnose some lymphoma subtypes including non-gastric MALT lymphoma, splenic marginal cell lymphoma, and mantle cell lymphoma[72].

CDKN2B deletion

cyclin dependent kinase inhibitor 2B

Background: CDKN2B encodes cyclin dependent kinase inhibitor 2B, a cell cycle regulator that controls G1/S progression[1,10]. CDKN2B, also known as p15/INK4B, belongs to a family of INK4 cyclin-dependent kinase inhibitors, which also includes CDKN2A (p16/INK4A), CDKN2C (p18/INK4C), and CDKN2D (p19/INK4D)[10]. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb[11,12,13]. CDKN2B is a tumor suppressor and aberrations in this gene commonly co-occur with CDKN2A[10]. Germline mutations in CDKN2B are linked to pancreatic cancer predisposition and familial renal cell carcinoma[1,32,33].

Alterations and prevalence: CDKN2B copy number loss is a frequently occurring somatic aberration that is observed in 55% of glioblastoma multiforme, 43% of mesothelioma, 35% of esophageal adenocarcinoma, 31% of bladder urothelial carcinoma, 29% of skin cutaneous melanoma, 28% of head and neck squamous cell carcinoma, 27% of pancreatic adenocarcinoma, 26% of lung squamous cell carcinoma, 25% of diffuse large B -cell lymphoma, 16% of lung adenocarcinoma, 15% of sarcoma, 14% of cholangiocarcinoma, 11% of stomach adenocarcinoma and brain lower grade glioma, 5% of liver hepatocellular carcinoma, 4% of adrenocortical carcinoma, breast invasive carcinoma, thymoma, and kidney renal papillary cell carcinoma, 3% of kidney renal clear cell carcinoma and ovarian serous cystadenocarcinoma, and 2% of uterine carcinosarcoma and kidney chromophobe[5,6]. Somatic mutations in CDKN2B are observed in 2% of uterine carcinosarcoma[5,6]. CDKN2B copy number loss is also observed in pediatric cancers, including 64% of childhood T-lymphoblastic leukemia/lymphoma, 37% of pediatric B-lymphoblastic leukemia/lymphoma, 25% of pediatric gliomas, 14% of pediatric bone cancers, 6% of embryonal tumors, and 2% of peripheral nervous system cancers[5,6]. Somatic mutations in CDKN2B are observed in less than 1% of bone cancer (1 in 327 cases)[5,6].

Potential relevance: Currently, no therapies are approved for CDKN2B aberrations. Homozygous deletion of CDKN2B is a molecular marker used in staging grade 4 pediatric IDH-mutant astrocytoma[23].

NTRK3 amplification

neurotrophic receptor tyrosine kinase 3

Background: The NTRK genes encode a family of neurotrophic receptor tyrosine kinases that function as receptors for nerve growth factors[89]. NTRKs are activated by different neurotrophins and are important for the development of the nervous system[89]. The NTRK1, 2 and 3 proteins are also known as tropomyosin-related kinases (TrkA, TrkB, TrkC) because NTRK1 was originally discovered as part of a chimeric fusion gene with tropomyosin-3 isolated from a human colon carcinoma cell line[90]. NTRKs are the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact tyrosine kinase domain combined with numerous fusion partner genes[91,92]. NTRK fusion kinases are constitutively active and lead to increased signaling through the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, or PLCγ/PKC pathways, promoting cell growth and proliferation[91,93].

Alterations and prevalence: NTRK fusions are infrequently observed in diverse pediatric and adult cancer types including glioma, glioblastoma, lung adenocarcinoma, colorectal carcinoma, thyroid cancer, and sarcoma[5,91,94,95,96,97,98]. In certain cancer subtypes, including melanoma, infantile fibrosarcoma, papillary thyroid carcinoma, and secretory carcinoma of the breast or salivary gland, NTRK fusions are more prevalent[91,98,99,100,101]. NTRK3 is amplified in 3% of mesothelioma, ovarian serous cystadenocarcinoma, sarcoma, stomach adenocarcinoma, and 2% of pancreatic adenocarcinoma, breast invasive carcinoma, cervical squamous cell carcinoma, and lung squamous cell carcinoma[5,6]. Somatic mutations in NTRK3 are observed in 11% of skin cutaneous melanoma, 8% of lung adenocarcinoma, uterine corpus endometrial carcinoma, 5% of lung squamous cell carcinoma, 4% of colorectal adenocarcinoma, 3% of stomach adenocarcinoma, cervical squamous cell carcinoma, cholangiocarcinoma, esophageal adenocarcinoma, and head and neck

Biomarker Descriptions (continued)

squamous cell carcinoma, and 2% of diffuse large B-cell lymphoma, adrenocortical carcinoma, liver hepatocellular carcinoma, uterine carcinosarcoma, bladder urothelial carcinoma, and kidney chromophobe[5,6]. Alterations in NTRK3 are rare in pediatric cancers[6]. NTRK3 is amplified in 1.5% of Wilms tumor (2 in 136 cases) and less than 1% of B-lymphoblastic leukemia/lymphoma (1 in 731 cases) and leukemia (1 in 250 cases)[6]. Somatic mutations in NTRK3 are observed in 3% of soft tissue sarcoma, 1% of glioma (3 in 297 cases), and less than 1% of bone cancer (2 in 327 cases), B-lymphoblastic leukemia/lymphoma (1 in 252 cases), leukemia (1 in 311 cases), and peripheral nervous system tumors (1 in 1158 cases)[6].

Potential relevance: The first-generation selective tropomyosin receptor kinase (TRK) inhibitor, larotrectinib[102], is approved (2018) for the treatment of adults and pediatric patients with any solid tumors harboring NTRK gene fusions and is the first approved small molecule inhibitor with a tissue agnostic indication. Entrectinib[103] is another first-generation TRK inhibitor approved (2019) for adults and pediatric patients with NTRK fusion-positive solid tumors as well as for adult patients with ROS1-positive non-small cell lung cancer (NSCLC). However, acquired resistance to first-generation NTRK inhibition is often mediated by the acquisition of solvent-front and gatekeeper mutations in the kinase domain[104]. Consequently, the second generation TRK inhibitor, repotrectinib[105], is approved by the FDA (2024) for the treatment of adult and pediatric patients with solid tumors that have an NTRK gene fusion. NTRK fusion is diagnostic of NTRK-rearranged spindle cell carcinoma as defined by the World Health Organization (WHO)[106].

FGF19 amplification

fibroblast growth factor 19

Background: The FGF19 gene encodes the fibroblast growth factor 19 protein, a member of the FGF protein family composed of twenty-two members[42,43]. With the exception of four non-signaling FGF memebers (FGF11-14), FGF proteins function as ligands and mediate the activation of the fibroblast growth factor receptor (FGFR) family of tyrosine kinases[42,43]. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLC/PKC, and JAK/STAT pathways thereby influencing cell proliferation, migration, and survival[44,45,46]. FGF19 is specifically observed to bind FGFR4 with increased affinity in the presence of the transmembrane protein klotho beta (KLB) which functions as a cofactor in FGF19 mediated FGFR4 activation[74,75]. FGF19-mediated aberrant signaling has been identified as an oncogenic driver in hepatocellular carcinoma[74,76].

Alterations and prevalence: FGF19 amplification is observed in 35% of esophageal adenocarcinoma, 23% of head and neck squamous cell carcinoma, 15% of breast invasive carcinoma, 13% of lung squamous cell carcinoma, 11% of cholangiocarcinoma and bladder urothelial carcinoma, 7% of stomach adenocarcinoma and liver hepatocellular carcinoma, 5% of skin cutaneous melanoma and ovarian serous cystadenocarcinoma, 3% of lung adenocarcinoma and cervical squamous cell carcinoma, and 2% of sarcoma, uterine corpus endometrial carcinoma, and prostate adenocarcinoma[5,6]. FGF19 aberrations are also observed in pediatric cancers[6]. FGF19 amplification is observed in 3% of peripheral nervous system cancers (3 in 91 cases), 2% of bone cancer (1 in 42 cases), and less than 1% of Wilms tumor (1 in 136 cases) and B-lymphoblastic leukemia/lymphoma (2 in 731 cases)[6]. Somatic mutations in FGF19 are observed in less than 1% of bone cancer (2 in 327 cases)[6].

Potential relevance: Currently, no therapies are approved for FGF19 aberrations. FGF19 overexpression is correlated with the development and tumor progression in hepatocellular carcinoma[77].

ASXL2 p.(R312*) c.934C>T

additional sex combs like 2, transcriptional regulator

Background: The ASXL2 gene encodes the ASXL transcriptional regulator 2 protein, a ligand-dependent co-activator and epigenetic scaffolding protein involved in transcriptional regulation[1,40]. ASXL2 belongs to the ASXL gene family, which also includes ASXL1 and ASXL3[40]. ASXL proteins contain a conserved C-terminal plant homeodomain (PHD), which facilitates interaction with DNA and histones[40]. ASXL2 influences chromatin remodeling and transcription through interaction with BAP1 as well as other transcriptional activators and repressors[40].

Alterations and prevalence: Somatic mutations in ASXL2 are observed in 8% of uterine corpus endometrial carcinoma and bladder urothelial carcinoma, 7% of skin cutaneous melanoma, 4% of colorectal adenocarcinoma, lung squamous cell carcinoma, and uterine carcinosarcoma[5,6]. ASXL2 mutations in acute myeloid leukemia (AML) are observed to co-occur with t(8;21)(q22;q22)/RUNX1::RUNX1T1[41]. ASXL2 deletions are observed in 4% diffuse large B-cell lymphoma (DLBCL) and 2% of uterine carcinosarcoma[5,6].

Potential relevance: Currently, no therapies are approved for ASXL2 aberrations. ASXL2 mutations have been shown to be associated with better prognosis in pediatric AML with t(8;21)[41].

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Biomarker Descriptions (continued)

FGF3 amplification

fibroblast growth factor 3

Background: The FGF3 gene encodes the fibroblast growth factor 3 protein, a member of the FGF protein family composed of twenty-two members[42,43]. With the exception of four non-signaling FGF memebers (FGF11-14), FGF proteins function as ligands and mediate the activation of the fibroblast growth factor receptor (FGFR) family of tyrosine kinases[42,43]. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLC/PKC, and JAK/STAT pathways thereby influencing cell proliferation, migration, and survival[44,45,46]. Specifically, FGF3 has been shown to bind to both FGFR1 and FGFR2[47,48]. Overexpression of FGF3 has been associated with certain tumor types including lung and liver cancers[49,50]. Additionally, constitutive ectopic expression has been suggested to promote tumorigenesis in vitro, supporting an oncogenic role for FGF3[48].

Alterations and prevalence: FGF3 amplification is observed in about 35% of esophageal cancer, 24% of head and neck cancer, 10-15% of invasive breast carcinoma, squamous lung, and bladder cancers as well as 5-10% of cholangiocarcinoma, melanoma, liver, ovarian and stomach cancers[5]. FGF3 overexpression is correlated with non-small cell lung cancer (NSCLC) development as well as tumor metastasis and recurrence in hepatocellular carcinoma[49,50].

Potential relevance: Currently, no therapies are approved for FGF3 aberrations.

FGF4 amplification

fibroblast growth factor 4

Background: The FGF4 gene encodes the fibroblast growth factor 4 protein, a member of the FGF protein family, which is composed of 22 members[1,43]. With the exception of four non-signaling FGF members (FGF11-14), FGF proteins function as ligands and mediate the activation of the fibroblast growth factor receptor (FGFR) family of tyrosine kinases[42,43]. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLC/PKC, and JAK/STAT pathways, thereby influencing cell proliferation, migration, and survival[44,45,46].

Alterations and prevalence: Amplifications in FGF4 are observed in various tumor types, but most frequently are found in up to 35% of esophageal adenocarcinoma, 24% of head and neck squamous cell carcinoma, 14% of breast invasive carcinoma, 12% of lung squamous cell carcinoma, 11% of cholangiocarcinoma, 10% of bladder urothelial carcinoma, 7% of stomach adenocarcinoma, and 5% of liver hepatocellular carcinoma[5,6]. FGF4 overexpression has been associated with Kaposi sarcoma lesions as well as testicular cancer[87,88].

Potential relevance: Currently, no therapies are approved for FGF4 aberrations.

MSH3 p.(A57Pfs*14) c.162_196delTGCAGCGGCCGCAGCGGCCGCAGCGCCCCCAGCGCinsCGCAGCG

mutS homolog 3

Background: The MSH3 gene encodes the mutS homolog 3 protein[1]. MSH3 heterodimerizes with MSH2 to form the MutSβ complex, an ATPase which functions in mismatch repair (MMR) by recognizing mismatches and initiating repair[2,3]. MSH3 is capable of interacting with proliferating cellular nuclear antigen (PCNA), which may facilitate MutSβ localization to DNA mispairs[2,3]. Mutations in MSH3 have been observed to be associated with microsatellite instability (MSI) in colon cancer[4].

Alterations and prevalence: Somatic mutations in MSH3 are observed in 9% of uterine corpus endometrial carcinoma, 4% of stomach adenocarcinoma, and 3% of skin cutaneous melanoma[5,6]. Biallelic deletion of MSH3 are observed in 3% of ovarian serous cystadenocarcinoma and 2% of prostate adenocarcinoma[5,6].

Potential relevance: Currently, no therapies are approved for MSH3 aberrations.

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[107]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[108,109]. 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[110]. 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[111]. 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)[111]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[112,113,114,115,116]. MSI-H is a hallmark of Lynch

Biomarker Descriptions (continued)

syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes[109]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[108,109,113,117].

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[108,109,118,119]. 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[118,119].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[120] (2014) and nivolumab[121] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[120] 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[120]. Dostarlimab[122] (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[114,123]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[124] (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[114,125,126]. 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[126]. 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[127,128]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[127,128].

NFE2L2 p.(W24C) c.72G>C

nuclear factor, erythroid 2 like 2

Background: The NFE2L2 gene encodes the nuclear factor, erythroid 2 like 2 transcription factor, a member of the basic leucine zipper protein family[1]. NFE2L2, also known as NRF2, is a proto-oncogene that activates transcription of genes with antioxidant response elements (ARE)[78]. NFE2L2 targets include genes involved in antioxidant response, drug metabolism, DNA repair, autophagy, cell survival, and proliferation[78,79]. NFE2L2 is negatively regulated by KEAP1, a Cul3 adaptor protein, that ubiquitinates NFE2L2[79].

Alterations and prevalence: Recurrent somatic mutations in NFE2L2 are observed in 14% of lung squamous cell carcinoma, 9% of esophageal adenocarcinoma, and 5% of head and neck squamous cell carcinoma[5,6]. Deletion of NFE2L2 exon 2 or exon 2 and 3 result in an isoform leading to the lack of the KEAP1 interacting domain, NFE2L2 stabilization, and expression of NFE2L2 targets such as HMOX1, G6PD, PDGFC, FGF2, and NQO1[78,80].

Potential relevance: Currently, no therapies are approved for NFE2L2 aberrations. The FDA has granted fast track designation (2022) to the mTORC 1/2 inhibitor, sapanisertib (CB-228)[81], for patients with NFE2L2 mutated, unresectable or metastatic squamous non-small cell lung cancer (NSCLC) who have received prior platinum-based chemotherapy and immune checkpoint inhibitor therapy.

TP53 p.(V157F) c.469G>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[51]. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential[52]. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[53,54].

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%)[5,6,55,56,57,58]. 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[5,6]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[59,60,61,62]. Alterations in TP53 are also observed in pediatric cancers[5,6]. 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)[5,6]. Biallelic loss

Biomarker Descriptions (continued)

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)[5,6].

Potential relevance: The small molecule p53 reactivator, PC14586[63] (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 activity, compounds that induce synthetic lethality are also under clinical evaluation[64,65]. TP53 mutations are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma[66]. 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)[67,68,69,70,71]. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[72]. 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[73].

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B[1]. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells[34]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[35]. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self[36,37,38]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B[39].

Alterations and prevalence: Somatic mutations in HLA-B are observed in 10% of diffuse large B-cell lymphoma (DLBCL), 5% of cervical squamous cell carcinoma and stomach adenocarcinoma, 4% of head and neck squamous cell carcinoma and colorectal adenocarcinoma, 3% of uterine cancer, and 2% of esophageal adenocarcinoma and skin cutaneous melanoma[5,6]. Biallelic loss of HLA-B is observed in 5% of DLBCL[5,6].

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

IDH2 amplification

isocitrate dehydrogenase (NADP(+)) 2, mitochondrial

Background: The IDH1 and IDH2 genes encode homologous isocitrate dehydrogenase enzymes that catalyze the conversion of isocitrate to α-ketoglutarate (α-KG)[129]. The IDH1 gene encodes the NADP+ dependent cytoplasmic isocitrate dehydrogenase enzyme; IDH2 encodes the mitochondrial isoform[129].

Alterations and prevalence: Recurrent somatic mutations in IDH1 and IDH2 are mutually exclusive and observed in several malignancies, including glioma, chondrosarcoma, intrahepatic cholangiocarcinoma, acute myeloid leukemia (AML), and myelodysplastic syndrome (MDS)[130]. Recurrent IDH2 variants include predominantly R140Q, R172K, and other substitutions at lower frequencies[131]. These gain-of-function variants confer neomorphic enzyme activity[132]. Although wild-type enzymatic activity is ablated, recurrent IDH2 variants catalyze the conversion of α-KG to D-2-hydroxyglutarate, an oncometabolite with diverse effects on cellular metabolism, epigenetic regulation, redox states, and DNA repair[129,133]. Recurrent IDH2 mutations are present in 10-20% of patients with AML and 5% of patients with MDS[134,135,136]. Alterations in IDH2 are rare in pediatric cancers[5,6]. Somatic mutations in IDH2 are observed in 1% of leukemia (4 in 311 cases) and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), glioma (1 in 297 cases), and bone cancer (1 in 327 cases)[5,6].

Potential relevance: The IDH1 and IDH2 inhibitor vorasidenib[137] is FDA-approved (2024) for the treatment of adults and children with Grade 2 astrocytoma or oligodendroglioma with IDH2 R172G/K/M/S/W mutations. Enasidenib[138] is FDA-approved (2017) for the treatment of AML patients with IDH2 R140G/L/Q/W and R172G/K/M/S/W mutations. Acquired resistance to enasidenib in AML has been linked to the emergence of Q316E or I319M mutations[139]. IDH2 mutations are associated with a favorable outcome in lower-grade gliomas, astrocytoma, and oligodendroglioma with 1p/19 codeletion[140,141]. IDH2 R172 and R140Q mutations are associated with poor risk in MDS[68,142]. IDH2 mutations are associated with inferior overall survival in polycythemia vera (PV) and essential thrombocythemia (ET), as well as inferior leukemia-free survival in primary myelofibrosis (PMF)[143,144]. Mutations in IDH2 are diagnostic of IDH-mutated astrocytoma and oligodendroglioma with 1p/19q-codeletion subtypes of central nervous system (CNS) tumors[66,140].

Disclaimer: The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. The data version is 2025.12(007).

Biomarker Descriptions (continued)

IGF1R amplification

insulin like growth factor 1 receptor

Background: The IGF1R gene encodes the insulin like growth factor 1 receptor, a type II receptor tyrosine kinase in the insulin receptor (IR) family along with IGF2R and INSR[82]. IR family proteins, including IGF1R, bind ligands insulin, insulin-like growth factors 1 and 2 (IGF-1/2), and serum insulin-like growth factor binding proteins (IGFBPs)[83]. IGF1R can homo- or heterodimerize with IGF2R to control ligand-induced activation[84]. After activation and autophosphorylation, docking sites allow for the binding of IRS1, IRS2, IRS3, IRS4, and SHC proteins, resulting in the activation of the the PI3K/AKT and RAS/RAF/MAPK signaling pathways[84]. IGF1R is ubiquitously expressed in normal tissues and plays a role in growth and glucose homeostasis[85]. In cancer, IGF1R overexpression is critical for anchorage-independent growth[85].

Alterations and prevalence: Somatic mutations in IGF1R are observed in 8% of uterine cancer, 6% of melanoma, 4% of stomach, and 3% of colorectal and bladder cancers[5,6]. Amplifications are observed in up to 5% of sarcoma, 4% of ovarian carcinoma, and 3% of breast, stomach, esophageal, and adrenocortical cancer[5,6].

Potential relevance: Currently, no therapies are approved for IGF1R aberrations. IGF1R localization has been implicated in chemotherapy resistance, with chemotherapy resistant cell lines presenting with significantly higher IGF1R nuclear expression[86].

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLCO1B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XPO1, ZNF217, ZNF429

Genes Assayed 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

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Genes Assayed (continued)

Genes Assayed for the Detection of Fusions

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

Genes Assayed with Full Exon Coverage

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

Relevant Therapy Summary

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

MTAP deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
MRTX-1719, chemotherapy	✖	✖	✖	✖	● (II/III)
AMG 193	✖	✖	✖	✖	● (I/II)
CTS-3497	✖	✖	✖	✖	● (I/II)
IDE397	✖	✖	✖	✖	● (I/II)
PH020-803	✖	✖	✖	✖	● (I/II)
TNG-456, abemaciclib	✖	✖	✖	✖	● (I/II)
TNG-462	✖	✖	✖	✖	● (I/II)
ABSK-131	✖	✖	✖	✖	● (I)
GH-56	✖	✖	✖	✖	● (I)
GTA-182	✖	✖	✖	✖	● (I)
HSK-41959	✖	✖	✖	✖	● (I)
ISM-3412	✖	✖	✖	✖	● (I)
MRTX-1719	✖	✖	✖	✖	● (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

MTAP deletion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
S-095035, TNG-462	✖	✖	✖	✖	● (I)
SYH-2039	✖	✖	✖	✖	● (I)

CDKN2A deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
palbociclib	✖	✖	✖	✖	● (II)
palbociclib, abemaciclib	✖	✖	✖	✖	● (II)
AMG 193	✖	✖	✖	✖	● (I/II)
ABSK-131	✖	✖	✖	✖	● (I)
CID-078	✖	✖	✖	✖	● (I)

CCND1 amplification

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

CDKN2B deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
palbociclib, abemaciclib	✖	✖	✖	✖	● (II)
CID-078	✖	✖	✖	✖	● (I)

NTRK3 amplification

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

FGF19 amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
TYRA-430	✖	✖	✖	✖	● (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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HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	***41.37%***
BRCA1	***LOH, 17q21.31(41197602-41276231)x3***
BRCA2	***LOH, 13q13.1(32890491-32972932)x2***
ATM	***LOH, 11q22.3(108098341-108236285)x2***
BRIP1	***LOH, 17q23.2(59760627-59938976)x3***
BRIP1	***SNV, S1031C, AF:0.12***
CDK12	***LOH, 17q12(37618286-37687611)x3***
CHEK1	***LOH, 11q24.2(125496639-125525271)x2***
CHEK2	***LOH, 22q12.1(29083868-29130729)x3***
FANCL	***LOH, 2p16.1(58386886-58468467)x3***
RAD51C	***LOH, 17q22(56769933-56811619)x3***
RAD51D	***LOH, 17q12(33427950-33446720)x3***

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 (6.2.4 data version 2025.12(007)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-11-25. NCCN information was sourced from www.nccn.org and is current as of 2025-11-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-11-25. ESMO information was sourced from www.esmo.org and is current as of 2025-11-03. Clinical Trials information is current as of 2025-11-03. 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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References

1. O'Leary et al. Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. Nucleic Acids Res. 2016 Jan 4;44(D1):D733-45. PMID: 26553804
2. Li. Mechanisms and functions of DNA mismatch repair. Cell Res. 2008 Jan;18(1):85-98. PMID: 18157157
3. Tamura et al. Genetic and genomic basis of the mismatch repair system involved in Lynch syndrome. Int J Clin Oncol. 2019 Sep;24(9):999-1011. PMID: 31273487
4. Ikeda et al. Close correlation between mutations of E2F4 and hMSH3 genes in colorectal cancers with microsatellite instability. Cancer Res. 1998 Feb 15;58(4):594-8. PMID: 9485005
5. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
6. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. Cancer Discov. 2012 May;2(5):401-4. PMID: 22588877
7. Harasawa et al. Chemotherapy targeting methylthioadenosine phosphorylase (MTAP) deficiency in adult T cell leukemia (ATL). Leukemia. 2002 Sep;16(9):1799-807. PMID: 12200696
8. Bertino et al. Targeting tumors that lack methylthioadenosine phosphorylase (MTAP) activity: current strategies. Cancer Biol Ther. 2011 Apr 1;11(7):627-32. PMID: 21301207
9. Katya et al. Cancer Dependencies: PRMT5 and MAT2A in MTAP/p16-Deleted Cancers. 10.1146/annurev-cancerbio-030419-033444
10. Xia et al. Dominant role of CDKN2B/p15INK4B of 9p21.3 tumor suppressor hub in inhibition of cell-cycle and glycolysis. Nat Commun. 2021 Apr 6;12(1):2047. PMID: 33824349
11. Scruggs et al. Loss of CDKN2B Promotes Fibrosis via Increased Fibroblast Differentiation Rather Than Proliferation. Am. J. Respir. Cell Mol. Biol. 2018 Aug;59(2):200-214. PMID: 29420051
12. Roussel. The INK4 family of cell cycle inhibitors in cancer. Oncogene. 1999 Sep 20;18(38):5311-7. PMID: 10498883
13. Aytac et al. Rb independent inhibition of cell growth by p15(INK4B). Biochem. Biophys. Res. Commun. 1999 Aug 27;262(2):534-8. PMID: 10462509
14. Hill et al. The genetics of melanoma: recent advances. Annu Rev Genomics Hum Genet. 2013;14:257-79. PMID: 23875803
15. Kim et al. The regulation of INK4/ARF in cancer and aging. Cell. 2006 Oct 20;127(2):265-75. PMID: 17055429
16. Sekulic et al. Malignant melanoma in the 21st century: the emerging molecular landscape. Mayo Clin. Proc. 2008 Jul;83(7):825-46. PMID: 18613999
17. Orlow et al. CDKN2A germline mutations in individuals with cutaneous malignant melanoma. J. Invest. Dermatol. 2007 May;127(5):1234-43. PMID: 17218939
18. Bartsch et al. CDKN2A germline mutations in familial pancreatic cancer. Ann. Surg. 2002 Dec;236(6):730-7. PMID: 12454511
19. Adib et al. CDKN2A Alterations and Response to Immunotherapy in Solid Tumors. Clin Cancer Res. 2021 Jul 15;27(14):4025-4035. PMID: 34074656
20. NCCN Guidelines® - NCCN-Mesothelioma: Peritoneal [Version 2.2026]
21. NCCN Guidelines® - NCCN-Mesothelioma: Pleural [Version 2.2026]
22. NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 1.2025]
23. Louis et al. cIMPACT-NOW update 6: new entity and diagnostic principle recommendations of the cIMPACT-Utrecht meeting on future CNS tumor classification and grading. Brain Pathol. 2020 Jul;30(4):844-856. PMID: 32307792
24. Longwen et al. Frequent genetic aberrations in the cell cycle related genes in mucosal melanoma indicate the potential for targeted therapy. J Transl Med. 2019 Jul 29;17(1):245. PMID: 31358010
25. Logan et al. PD-0332991, a potent and selective inhibitor of cyclin-dependent kinase 4/6, demonstrates inhibition of proliferation in renal cell carcinoma at nanomolar concentrations and molecular markers predict for sensitivity. Anticancer Res. 2013 Aug;33(8):2997-3004. PMID: 23898052
26. von Witzleben et al. Preclinical Characterization of Novel Chordoma Cell Systems and Their Targeting by Pharmocological Inhibitors of the CDK4/6 Cell-Cycle Pathway. Cancer Res. 2015 Sep 15;75(18):3823-31. PMID: 26183925
27. Cen et al. p16-Cdk4-Rb axis controls sensitivity to a cyclin-dependent kinase inhibitor PD0332991 in glioblastoma xenograft cells. Neuro-oncology. 2012 Jul;14(7):870-81. PMID: 22711607
28. Vitzthum et al. The role of p16 as a biomarker in nonoropharyngeal head and neck cancer. Oncotarget. 2018 Sep 7;9(70):33247-33248. PMID: 30279955
29. Chung et al. p16 protein expression and human papillomavirus status as prognostic biomarkers of nonoropharyngeal head and neck squamous cell carcinoma. J. Clin. Oncol. 2014 Dec 10;32(35):3930-8. PMID: 25267748

Disclaimer: The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. The data version is 2025.12(007).

References (continued)

30. Bryant et al. Prognostic Role of p16 in Nonoropharyngeal Head and Neck Cancer. J. Natl. Cancer Inst. 2018 Dec 1;110(12):1393-1399. PMID: 29878161
31. Stephen et al. Significance of p16 in Site-specific HPV Positive and HPV Negative Head and Neck Squamous Cell Carcinoma. Cancer Clin Oncol. 2013;2(1):51-61. PMID: 23935769
32. Jafri et al. Germline Mutations in the CDKN2B Tumor Suppressor Gene Predispose to Renal Cell Carcinoma. Cancer Discov.2015 Jul;5(7):723-9. PMID: 25873077
33. Tu et al. CDKN2B deletion is essential for pancreatic cancer development instead of unmeaningful co-deletion due to juxtaposition to CDKN2A. Oncogene. 2018 Jan 4;37(1):128-138. PMID: 28892048
34. Hulpke et al. The MHC I loading complex: a multitasking machinery in adaptive immunity. Trends Biochem Sci. PMID: 23849087
35. Adams et al. The adaptable major histocompatibility complex (MHC) fold: structure and function of nonclassical and MHC class I-like molecules. Annu Rev Immunol. 2013;31:529-61. PMID: 23298204
36. Rossjohn et al. T cell antigen receptor recognition of antigen-presenting molecules. Annu Rev Immunol. 2015;33:169-200. PMID: 25493333
37. Parham. MHC class I molecules and KIRs in human history, health and survival. Nat Rev Immunol. 2005 Mar;5(3):201-14. PMID: 15719024
38. Sidney et al. HLA class I supertypes: a revised and updated classification. BMC Immunol. 2008 Jan 22;9:1. PMID: 18211710
39. Cornel et al. MHC Class I Downregulation in Cancer: Underlying Mechanisms and Potential Targets for Cancer Immunotherapy. Cancers (Basel). 2020 Jul 2;12(7). PMID: 32630675
40. Katoh. Functional and cancer genomics of ASXL family members. Br. J. Cancer. 2013 Jul 23;109(2):299-306. PMID: 23736028
41. Yamato et al. ASXL2 mutations are frequently found in pediatric AML patients with t(8;21)/ RUNX1-RUNX1T1 and associated with a better prognosis. Genes Chromosomes Cancer. 2017 May;56(5):382-393. PMID: 28063196
42. Beenken et al. The FGF family: biology, pathophysiology and therapy. Nat Rev Drug Discov. 2009 Mar;8(3):235-53. PMID: 19247306
43. Ornitz et al. The Fibroblast Growth Factor signaling pathway. Wiley Interdiscip Rev Dev Biol . May-Jun 2015;4(3):215-66. doi: 10.1002/wdev.176. PMID: 25772309
44. Babina et al. Advances and challenges in targeting FGFR signalling in cancer. Nat. Rev. Cancer. 2017 May;17(5):318-332. PMID: 28303906
45. Ahmad et al. Mechanisms of FGFR-mediated carcinogenesis. Biochim. Biophys. Acta. 2012 Apr;1823(4):850-60. PMID: 22273505
46. Sarabipour et al. Mechanism of FGF receptor dimerization and activation. Nat Commun. 2016 Jan 4;7:10262. doi: 10.1038/ncomms10262. PMID: 26725515
47. Itoh et al. Evolution of the Fgf and Fgfr gene families. Trends Genet. 2004 Nov;20(11):563-9. PMID: 15475116
48. Mathieu et al. Receptor binding and mitogenic properties of mouse fibroblast growth factor 3. Modulation of response by heparin. J. Biol. Chem. 1995 Oct 13;270(41):24197-203. PMID: 7592624
49. Tai et al. Co-overexpression of fibroblast growth factor 3 and epidermal growth factor receptor is correlated with the development of nonsmall cell lung carcinoma. Cancer. 2006 Jan 1;106(1):146-55. PMID: 16329133
50. Hu et al. Up-regulation of fibroblast growth factor 3 is associated with tumor metastasis and recurrence in human hepatocellular carcinoma. Cancer Lett. 2007 Jul 8;252(1):36-42. PMID: 17215076
51. Nag et al. The MDM2-p53 pathway revisited. J Biomed Res. 2013 Jul;27(4):254-71. PMID: 23885265
52. Muller et al. Mutant p53 in cancer: new functions and therapeutic opportunities. Cancer Cell. 2014 Mar 17;25(3):304-17. PMID: 24651012
53. Olivier et al. TP53 mutations in human cancers: origins, consequences, and clinical use. Cold Spring Harb Perspect Biol. 2010 Jan;2(1):a001008. PMID: 20182602
54. Guha et al. Inherited TP53 Mutations and the Li-Fraumeni Syndrome. Cold Spring Harb Perspect Med. 2017 Apr 3;7(4). PMID: 28270529
55. Peter S et al. Comprehensive genomic characterization of squamous cell lung cancers. Nature. 2012 Sep 27;489(7417):519-25. PMID: 22960745
56. Cancer Genome Atlas Network. Comprehensive genomic characterization of head and neck squamous cell carcinomas. Nature. 2015 Jan 29;517(7536):576-82. PMID: 25631445
57. Campbell et al. Distinct patterns of somatic genome alterations in lung adenocarcinomas and squamous cell carcinomas. Nat. Genet. 2016 Jun;48(6):607-16. PMID: 27158780

Disclaimer: The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. The data version is 2025.12(007).

References (continued)

58. Cancer Genome Atlas Research Network. Integrated genomic characterization of oesophageal carcinoma. Nature. 2017 Jan 12;541(7636):169-175. doi: 10.1038/nature20805. Epub 2017 Jan 4. PMID: 28052061
59. Olivier et al. The IARC TP53 database: new online mutation analysis and recommendations to users. Hum. Mutat. 2002 Jun;19(6):607-14. PMID: 12007217
60. Rivlin et al. Mutations in the p53 Tumor Suppressor Gene: Important Milestones at the Various Steps of Tumorigenesis. Genes Cancer. 2011 Apr;2(4):466-74. PMID: 21779514
61. Petitjean et al. TP53 mutations in human cancers: functional selection and impact on cancer prognosis and outcomes. Oncogene. 2007 Apr 2;26(15):2157-65. PMID: 17401424
62. Soussi et al. Recommendations for analyzing and reporting TP53 gene variants in the high-throughput sequencing era. Hum. Mutat. 2014 Jun;35(6):766-78. PMID: 24729566
63. https://www.globenewswire.com/news-release/2020/10/13/2107498/0/en/PMV-Pharma-Granted-FDA-Fast-Track-Designation-of-PC14586-for-the-Treatment-of-Advanced-Cancer-Patients-that-have-Tumors-with-a-p53-Y220C-Mutation.html
64. Parrales et al. Targeting Oncogenic Mutant p53 for Cancer Therapy. Front Oncol. 2015 Dec 21;5:288. doi: 10.3389/fonc.2015.00288. eCollection 2015. PMID: 26732534
65. Zhao et al. Molecularly targeted therapies for p53-mutant cancers. Cell. Mol. Life Sci. 2017 Nov;74(22):4171-4187. PMID: 28643165
66. Louis et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021 Aug 2;23(8):1231-1251. PMID: 34185076
67. Döhner et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022 Sep 22;140(12):1345-1377. PMID: 35797463
68. NCCN Guidelines® - NCCN-Myelodysplastic Syndromes [Version 1.2026]
69. NCCN Guidelines® - NCCN-Myeloproliferative Neoplasms [Version 2.2025]
70. NCCN Guidelines® - NCCN-Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma [Version 1.2026]
71. NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 2.2025]
72. NCCN Guidelines® - NCCN-B-Cell Lymphomas [Version 3.2025]
73. Bernard et al. Implications of TP53 allelic state for genome stability, clinical presentation and outcomes in myelodysplastic syndromes. Nat. Med. 2020 Aug 3. PMID: 32747829
74. Repana et al. Targeting FGF19/FGFR4 Pathway: A Novel Therapeutic Strategy for Hepatocellular Carcinoma. Diseases. 2015 Oct 28;3(4):294-305. PMID: 28943626
75. Goetz et al. Molecular insights into the klotho-dependent, endocrine mode of action of fibroblast growth factor 19 subfamily members. Mol. Cell. Biol. 2007 May;27(9):3417-28. PMID: 17339340
76. Lu et al. Fibroblast Growth Factor Receptor 4 (FGFR4) Selective Inhibitors as Hepatocellular Carcinoma Therapy: Advances and Prospects. J. Med. Chem. 2018 Nov 16. PMID: 30403487
77. Miura et al. Fibroblast growth factor 19 expression correlates with tumor progression and poorer prognosis of hepatocellular carcinoma. BMC Cancer. 2012 Feb 6;12:56. doi: 10.1186/1471-2407-12-56. PMID: 22309595
78. Rojo de la Vega et al. NRF2 and the Hallmarks of Cancer. Cancer Cell. 2018 Jul 9;34(1):21-43. PMID: 29731393
79. Suzuki et al. Toward clinical application of the Keap1-Nrf2 pathway. Trends Pharmacol. Sci. 2013 Jun;34(6):340-6. PMID: 23664668
80. Goldstein et al. Recurrent Loss of NFE2L2 Exon 2 Is a Mechanism for Nrf2 Pathway Activation in Human Cancers. Cell Rep. 2016 Sep 6;16(10):2605-2617. PMID: 27568559
81. https://ir.calithera.com//news-releases/news-release-details/calithera-receives-fda-fast-track-designation-sapanisertib
82. Adams et al. Structure and function of the type 1 insulin-like growth factor receptor. Cell. Mol. Life Sci. 2000 Jul;57(7):1050-93. PMID: 10961344
83. Yuan et al. Function of insulin-like growth factor 1 receptor in cancer resistance to chemotherapy. Oncol Lett. 2018 Jan;15(1):41-47. PMID: 29285186
84. Chitnis et al. The type 1 insulin-like growth factor receptor pathway. Clin. Cancer Res. 2008 Oct 15;14(20):6364-70. PMID: 18927274
85. Chen et al. IGF-1R as an anti-cancer target--trials and tribulations. Chin J Cancer. 2013 May;32(5):242-52. PMID: 23601239
86. Denduluri et al. Insulin-like growth factor (IGF) signaling in tumorigenesis and the development of cancer drug resistance. Genes Dis. 2015 Mar 1;2(1):13-25. PMID: 25984556

Disclaimer: The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. The data version is 2025.12(007).

References (continued)

87. Kiuru-Kuhlefelt et al. FGF4 and INT2 oncogenes are amplified and expressed in Kaposi's sarcoma. Mod Pathol. 2000 Apr;13(4):433-7. PMID: 10786811
88. Suzuki et al. Predominant expression of fibroblast growth factor (FGF) 8, FGF4, and FGF receptor 1 in nonseminomatous and highly proliferative components of testicular germ cell tumors. Virchows Arch. 2001 Nov;439(5):616-21. PMID: 11764380
89. Bibel et al. Neurotrophins: key regulators of cell fate and cell shape in the vertebrate nervous system. Genes Dev. 2000 Dec 1;14(23):2919-37. PMID: 11114882
90. Martin-Zanca et al. A human oncogene formed by the fusion of truncated tropomyosin and protein tyrosine kinase sequences. Nature. 1986 Feb 27-Mar 5;319(6056):743-8. PMID: 2869410
91. Amatu et al. NTRK gene fusions as novel targets of cancer therapy across multiple tumour types. ESMO Open. 2016 Mar 18;1(2):e000023. eCollection 2016. PMID: 27843590
92. Lange et al. Inhibiting TRK Proteins in Clinical Cancer Therapy. Cancers (Basel). 2018 Apr 4;10(4). PMID: 29617282
93. Vaishnavi et al. TRKing down an old oncogene in a new era of targeted therapy. Cancer Discov. 2015 Jan;5(1):25-34. PMID: 25527197
94. Kim et al. NTRK1 fusion in glioblastoma multiforme. PLoS ONE. 2014;9(3):e91940. PMID: 24647444
95. Gatalica et al. Molecular characterization of cancers with NTRK gene fusions. Mod. Pathol. 2019 Jan;32(1):147-153. PMID: 30171197
96. Vaishnavi et al. Oncogenic and drug-sensitive NTRK1 rearrangements in lung cancer. Nat. Med. 2013 Nov;19(11):1469-1472. PMID: 24162815
97. O'Haire et al. Systematic review of NTRK 1/2/3 fusion prevalence pan-cancer and across solid tumours. Sci Rep. 2023 Mar 13;13(1):4116. PMID: 36914665
98. Blauel et al. The promise of TRK inhibitors in pediatric cancers with NTRK fusions. Cancer Genet. 2022 Apr;262-263:71-79. PMID: 35108663
99. Rubin et al. Congenital mesoblastic nephroma t(12;15) is associated with ETV6-NTRK3 gene fusion: cytogenetic and molecular relationship to congenital (infantile) fibrosarcoma. Am. J. Pathol. 1998 Nov;153(5):1451-8. PMID: 9811336
100. Brzeziańska et al. Molecular analysis of the RET and NTRK1 gene rearrangements in papillary thyroid carcinoma in the Polish population. Mutat. Res. 2006 Jul 25;599(1-2):26-35. PMID: 16483615
101. Wu et al. The genomic landscape of diffuse intrinsic pontine glioma and pediatric non-brainstem high-grade glioma. Nat. Genet. 2014 May;46(5):444-450. PMID: 24705251
102. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/210861s012lbl.pdf
103. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/212725s011lbl.pdf
104. Fuse et al. Mechanisms of Resistance to NTRK Inhibitors and Therapeutic Strategies in NTRK1-Rearranged Cancers. Mol. Cancer Ther. 2017 Oct;16(10):2130-2143. PMID: 28751539
105. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218213s001lbl.pdf
106. Demetri et al. Diagnosis and management of tropomyosin receptor kinase (TRK) fusion sarcomas: expert recommendations from the World Sarcoma Network. Ann Oncol. 2020 Nov;31(11):1506-1517. PMID: 32891793
107. Lander et al. Initial sequencing and analysis of the human genome. Nature. 2001 Feb 15;409(6822):860-921. PMID: 11237011
108. Baudrin et al. Molecular and Computational Methods for the Detection of Microsatellite Instability in Cancer. Front Oncol. 2018 Dec 12;8:621. doi: 10.3389/fonc.2018.00621. eCollection 2018. PMID: 30631754
109. Nojadeh et al. Microsatellite instability in colorectal cancer. EXCLI J. 2018;17:159-168. PMID: 29743854
110. Saeed et al. Microsatellites in Pursuit of Microbial Genome Evolution. Front Microbiol. 2016 Jan 5;6:1462. doi: 10.3389/fmicb.2015.01462. eCollection 2015. PMID: 26779133
111. Boland et al. A National Cancer Institute Workshop on Microsatellite Instability for cancer detection and familial predisposition: development of international criteria for the determination of microsatellite instability in colorectal cancer. Cancer Res. 1998 Nov 15;58(22):5248-57. PMID: 9823339
112. Halford et al. Low-level microsatellite instability occurs in most colorectal cancers and is a nonrandomly distributed quantitative trait. Cancer Res. 2002 Jan 1;62(1):53-7. PMID: 11782358
113. Imai et al. Carcinogenesis and microsatellite instability: the interrelationship between genetics and epigenetics. Carcinogenesis. 2008 Apr;29(4):673-80. PMID: 17942460
114. NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]
115. Pawlik et al. Colorectal carcinogenesis: MSI-H versus MSI-L. Dis. Markers. 2004;20(4-5):199-206. PMID: 15528785

Disclaimer: The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. The data version is 2025.12(007).

References (continued)

116. Lee et al. Low-Level Microsatellite Instability as a Potential Prognostic Factor in Sporadic Colorectal Cancer. Medicine (Baltimore). 2015 Dec;94(50):e2260. PMID: 26683947
117. Latham et al. Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. J. Clin. Oncol. 2019 Feb 1;37(4):286-295. PMID: 30376427
118. Cortes-Ciriano et al. A molecular portrait of microsatellite instability across multiple cancers. Nat Commun. 2017 Jun 6;8:15180. doi: 10.1038/ncomms15180. PMID: 28585546
119. Bonneville et al. Landscape of Microsatellite Instability Across 39 Cancer Types. JCO Precis Oncol. 2017;2017. PMID: 29850653
120. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125514s178lbl.pdf
121. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125554s131lbl.pdf
122. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761174s009lbl.pdf
123. NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]
124. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125377s136lbl.pdf
125. Ribic et al. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. N. Engl. J. Med. 2003 Jul 17;349(3):247-57. PMID: 12867608
126. Klingbiel et al. Prognosis of stage II and III colon cancer treated with adjuvant 5-fluorouracil or FOLFIRI in relation to microsatellite status: results of the PETACC-3 trial. Ann. Oncol. 2015 Jan;26(1):126-32. PMID: 25361982
127. Hermel et al. The Emerging Role of Checkpoint Inhibition in Microsatellite Stable Colorectal Cancer. J Pers Med. 2019 Jan 16;9(1). PMID: 30654522
128. Ciardiello et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy. Cancer Treat. Rev. 2019 Jun;76:22-32. PMID: 31079031
129. Molenaar et al. Wild-type and mutated IDH1/2 enzymes and therapy responses. Oncogene. 2018 Apr;37(15):1949-1960. PMID: 29367755
130. Yan et al. IDH1 and IDH2 mutations in gliomas. N. Engl. J. Med. 2009 Feb 19;360(8):765-73. PMID: 19228619
131. Waitkus et al. Biological Role and Therapeutic Potential of IDH Mutations in Cancer. Cancer Cell. 2018 Aug 13;34(2):186-195. PMID: 29805076
132. Dang et al. Cancer-associated IDH1 mutations produce 2-hydroxyglutarate. Nature. 2009 Dec 10;462(7274):739-44. PMID: 19935646
133. Ward et al. The common feature of leukemia-associated IDH1 and IDH2 mutations is a neomorphic enzyme activity converting alpha-ketoglutarate to 2-hydroxyglutarate. Cancer Cell. 2010 Mar 16;17(3):225-34. PMID: 20171147
134. Paschka et al. IDH1 and IDH2 mutations are frequent genetic alterations in acute myeloid leukemia and confer adverse prognosis in cytogenetically normal acute myeloid leukemia with NPM1 mutation without FLT3 internal tandem duplication. J. Clin. Oncol. 2010 Aug 1;28(22):3636-43. PMID: 20567020
135. Chou et al. The prognostic impact and stability of Isocitrate dehydrogenase 2 mutation in adult patients with acute myeloid leukemia. Leukemia. 2011 Feb;25(2):246-53. PMID: 21079611
136. Marcucci et al. IDH1 and IDH2 gene mutations identify novel molecular subsets within de novo cytogenetically normal acute myeloid leukemia: a Cancer and Leukemia Group B study. J. Clin. Oncol. 2010 May 10;28(14):2348-55. PMID: 20368543
137. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/218784s002lbl.pdf
138. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/209606s007lbl.pdf
139. Intlekofer et al. Acquired resistance to IDH inhibition through trans or cis dimer-interface mutations. Nature. 2018 Jul;559(7712):125-129. PMID: 29950729
140. NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2025]
141. Cancer Genome Atlas Research Network. Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. N Engl J Med. 2015 Jun 25;372(26):2481-98. doi: 10.1056/NEJMoa1402121. Epub 2015 Jun 10. PMID: 26061751
142. Houillier et al. IDH1 or IDH2 mutations predict longer survival and response to temozolomide in low-grade gliomas. Neurology. 2010 Oct 26;75(17):1560-6. PMID: 20975057
143. Vannucchi et al. Mutations and prognosis in primary myelofibrosis. Leukemia. 2013 Sep;27(9):1861-9. PMID: 23619563
144. Tefferi et al. IDH1 and IDH2 mutation studies in 1473 patients with chronic-, fibrotic- or blast-phase essential thrombocythemia, polycythemia vera or myelofibrosis. Leukemia. 2010 Jul;24(7):1302-9. PMID: 20508616
145. Malumbres et al. Cell cycle, CDKs and cancer: a changing paradigm. Nat. Rev. Cancer. 2009 Mar;9(3):153-66. PMID: 19238148

Disclaimer: The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. The data version is 2025.12(007).

References (continued)

146. Koyama-Nasu et al. The critical role of cyclin D2 in cell cycle progression and tumorigenicity of glioblastoma stem cells. Oncogene. 2013 Aug 15;32(33):3840-5. PMID: 22964630
147. Ding et al. Prognostic role of cyclin D2/D3 in multiple human malignant neoplasms: A systematic review and meta-analysis. Cancer Med. 2019 Jun;8(6):2717-2729. PMID: 30950241
148. Bartek et al. Pathways governing G1/S transition and their response to DNA damage. FEBS Lett. 2001 Feb 16;490(3):117-22. PMID: 11223026
149. Shan et al. Cyclin D1 overexpression correlates with poor tumor differentiation and prognosis in gastric cancer. Oncol Lett. 2017 Oct;14(4):4517-4526. PMID: 28943959
150. Cancer Genome Atlas Research et al. Integrated genomic characterization of endometrial carcinoma. Nature. 2013 May 2;497(7447):67-73. PMID: 23636398
151. Beà et al. Landscape of somatic mutations and clonal evolution in mantle cell lymphoma. Proc. Natl. Acad. Sci. U.S.A. 2013 Nov 5;110(45):18250-5. PMID: 24145436
152. Diehl et al. Glycogen synthase kinase-3beta regulates cyclin D1 proteolysis and subcellular localization. Genes Dev. 1998 Nov 15;12(22):3499-511. PMID: 9832503
153. Alt et al. Phosphorylation-dependent regulation of cyclin D1 nuclear export and cyclin D1-dependent cellular transformation. Genes Dev. 2000 Dec 15;14(24):3102-14. PMID: 11124803
154. Moreno-Bueno et al. Cyclin D1 gene (CCND1) mutations in endometrial cancer. Oncogene. 2003 Sep 4;22(38):6115-8. PMID: 12955092
155. Benzeno et al. Identification of mutations that disrupt phosphorylation-dependent nuclear export of cyclin D1. Oncogene. 2006 Oct 12;25(47):6291-303. PMID: 16732330
156. Kim et al. Nuclear cyclin D1: an oncogenic driver in human cancer. J. Cell. Physiol. 2009 Aug;220(2):292-6. PMID: 19415697
157. Jares et al. Genetic and molecular pathogenesis of mantle cell lymphoma: perspectives for new targeted therapeutics. Nat. Rev. Cancer. 2007 Oct;7(10):750-62. PMID: 17891190

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